Structure and Reactivity in the Heterotropilidene Series and Other Studies

By

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DEDICATION

This dissertation is dedicated to all of the people, places, animals, and things which have made the past four years a worthwhile experience in Life.

ACKNOWLEDGEMENTS

The author wishes to thank his research director, Prof. Merle A. Battiste, for excellent guidance on this project, helpful discussions, and, most of all, moral support when it was needed. The author would also like to thank the Palenik Group, especially M. Mathew, for the generous use of their x-ray facilities and cheerful help on structure 67; Dr. R.W. King for the computer solutions of the NMR spectra of compounds 79 and 80; and Dr. R. Rehburg for samples of compounds 2, 3, 10, and 11 and the excellent groundwork done on the project before the author took over.

The author also wishes to recognize and thank The Ghetto, Alpha Chi Sigma and its members, especially S.R., S.W., P.F.E., J.H., M.K., H.J., and R.K.; 1743, SCL, L&N, T.E.H., The Zoo, The Rat, R.W.C.V., C.C.V., R.L., Huntsville, Nashville, and all of the other people, places, animals, and things whose sheer volume space does not permit mention of but which have made the past four years more than just a pure academic experience.

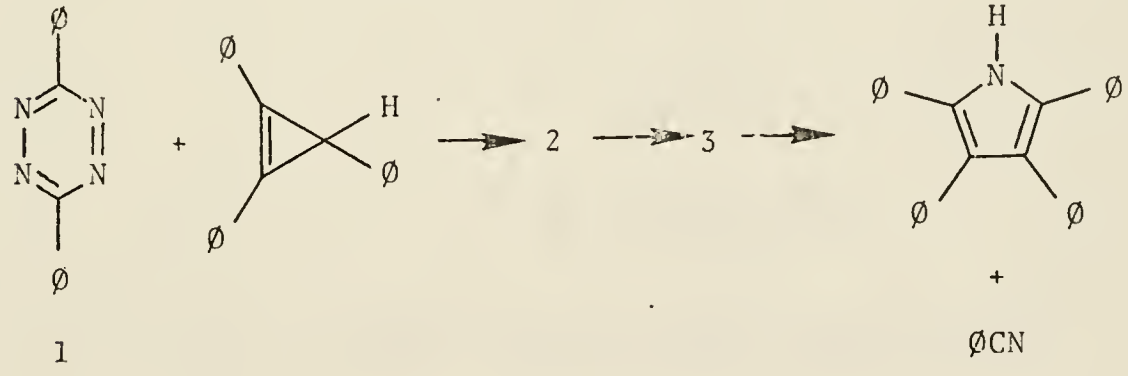
The author also wishes to thank his wife, Ann, for providing moral support when it was needed and his son, Robbie, for being so patient these past four years.

"I remember when this whole thing began
No talk of God then - we called you a man."

Jesus Christ Superstar, 1970

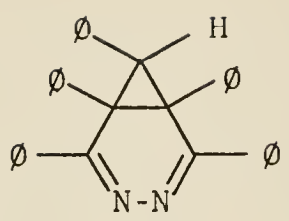
PREFACE

As part of a general study of the Diels-Alder reaction of tetrazines with alkenes, it was discovered independently in 1966 by Sauer and Heinrichs,[1] and Battiste and Barton[2] that sym-triphenylcyclopropene reacts with 3,6-diphenyl-1,2,4,5-tetrazine (1) at 20 to 78° to produce a yellow compound (2) $C_{35}H_{26}N_2$ which, on heating (100° or greater), isomerizes to an almost colorless compound (3) which, on further heating (230°), decomposes into benzonitrile and sym-tetraphenylpyrrole. The results of both investigations are summarized in Scheme 1.



Scheme 1

Sauer was of the opinion that 2 is in the diazanorcaradiene form, 1,2,5,6,7-pentaphenyl-3,4-diazabicyclo[4.1.0]-hepta-2,4-diene (4). Battiste, however, argued that 2 should be described as 3,4,5,6,7-pentaphenyl-5H-1,2-diazepine (5).



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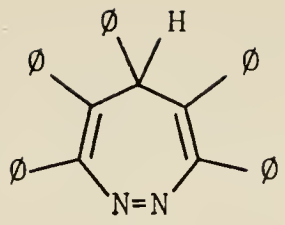

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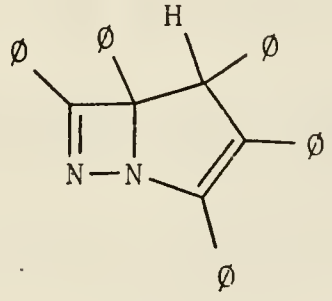
Both Sauer and Battiste agreed that 2,5-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (6)[1,2,3] and 2,5,7-triphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (7)[4] and other diazanorcaradienes with no phenyls at C-1 and C-6 exist exclusively in the diazanorcaradiene form at room temperature.

Sauer based his argument for 4 on the fact that the UV spectrum of 2 is quite similar to that of 6 even though Maier[3] had previously shown that substituents in the 1- and 6-positions imposed steric restrictions on the phenyls in the 2- and 5-positions causing a hypsochromic shift in the ultraviolet. Thus, there was some doubt as to whether the UV of 4 and the UV of 6 could be compared.

Battiste suggested that the low-field position of the only non-aromatic absorption in the NMR spectrum of 2 indicated an allylic type signal rather than a cyclopropyl type signal. Battiste also felt that the phenyls in the 1- and 6-positions would facilitate the disrotatory opening of the initially formed 4 to give a diazacycloheptatriene system.

Sauer proposed that product 3 is the result of disrotatory ring opening of 4 to give the 5H-diazepine 5 or one of its hydrogen-shifted (except to nitrogen) products. Again Sauer based his arguments on the UV spectrum of 3, citing extended conjugation as being responsible for the spectrum.

On the basis of its facile conversion to tetraphenylpyrrole and benzonitrile, Battiste tentatively proposed the bicyclic structure 8 for isomer 3.



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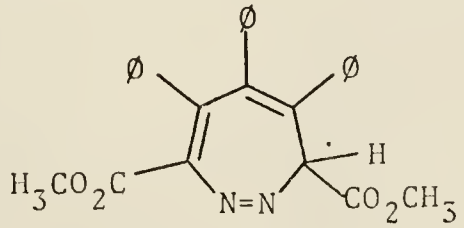
The reaction of dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (9) with sym-triphenylcyclopropene gives products 10 and 11 which are analogous to 2 and 3 above. Since the product 11 shows nonequivalent ester methyls in the NMR, Sauer[5] assigned to it the structure 12.



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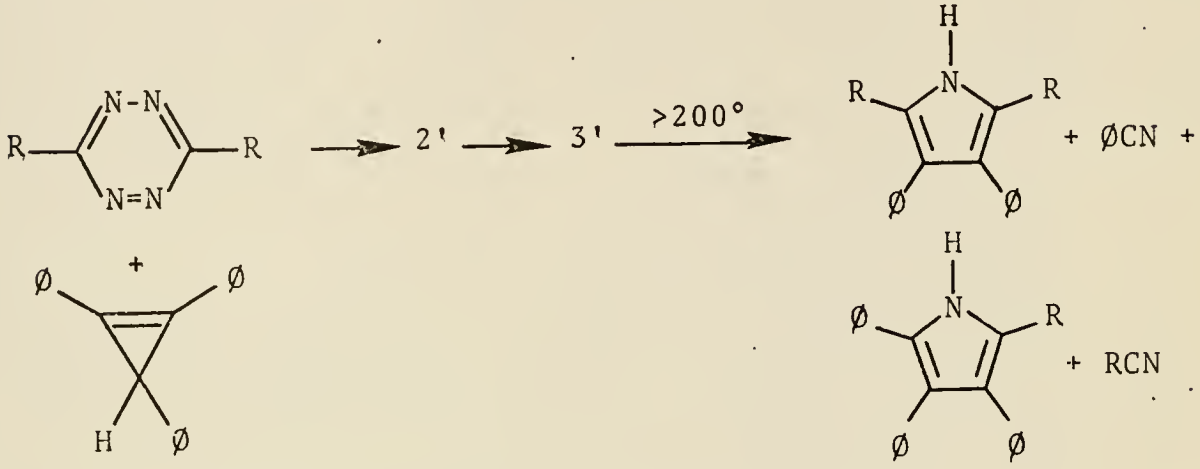
It was shown by Rehburg and Battiste[6] that mixtures of pyrroles are obtained from diaza species similar to 3 or 11 when the tetrazine has substituted phenyls, methyls, or carbomethoxy groups attached to it as illustrated below in Scheme 2.

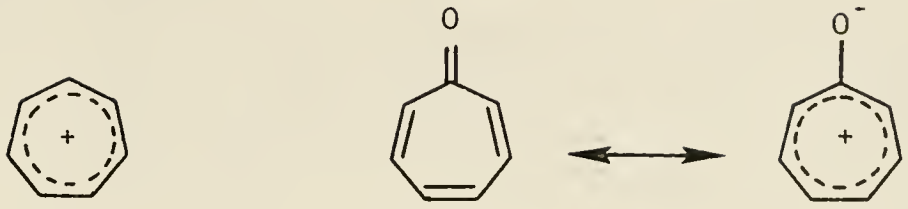


R = CH_3, p-H_3C-C_6H_4, CO_2CH_3

Scheme 2

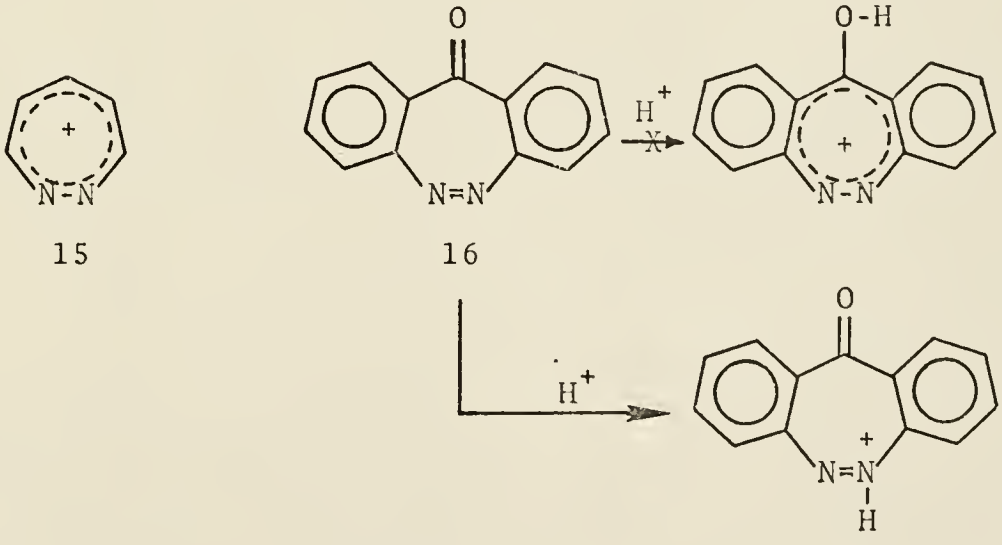
At the time this work was initiated, it still was not known definitely whether 2 existed as diazanorcaradiene or 5H-diazepine, nor had the structure of 3 been established. Also, no mechanistic details on the conversion of 2 to 3 were available. Chapter I deals in some detail with the structures of 2 and 3 and the mechanism of the thermal isomerization of 2 to 3.

When this investigation was begun, the aromaticity and stability of the cycloheptatrienylium or tropylium cation (13) were well known.[7,8] Also, the aromaticity of cycloheptatrienone or tropone (14) was well-documented.[7,8]



13 14

By contrast, the analogous 1,2-diazacycloheptatrienylium cation (15) was a complete unknown at the beginning of this work. Only one 1,2-diazatropone derivative, 16, had been reported.[9] In acid, 16 did not protonate on oxygen to form the aromatic dibenzohydroxydiazatropylium cation, but, rather, it protonated on nitrogen to form an amine salt as illustrated in Scheme 3.



Scheme 3

Since at the beginning of this investigation it was thought that compounds such as 2 existed in the open 5H-diazepine form, the possibility of synthesizing the diaza

analogs of the tropylium cation and tropone appeared to be a feasible project. The diazatropylium cation-diazatropone problem will be dealt with in Chapter IV.

Also, the tetrazines which are used in the synthesis of many of the diazanorcaradienes and diazepines present themselves as an interesting heteroaromatic series. The spectral properties of some of the more interesting members of this series will be examined in some detail along with members of related aromatic systems in Chapter III.

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Abstract of Dissertation Presented to the Graduate Council of the University of Florida in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

STRUCTURE AND REACTIVITY IN THE HETEROTROPILIDENE SERIES AND OTHER STUDIES

By

Robert Merrifield White

March, 1972

Chairman: M.A. Battiste
Major Department: Chemistry

It has been found that the reaction between sym-triphenylcyclopropene and 3,6-diphenyl-1,2,4,5-tetrazine produces 1,2,5,6,7-pentaphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene or pentaphenyldiazanorcaradiene which, on heating, isomerizes to 3,4,5,6,7-pentaphenyl-4H-1,2-diazepine as determined by x-ray studies. It has been demonstrated conclusively that pentaphenyldiazanorcaradiene rearranges to the 4H-diazepine via a carbon-shift rather than a hydrogen-shift mechanism. The exact mechanism of the carbon shift was not determined. Preliminary work on the decomposition of 4H-diazepines into pyrroles and benzonitriles has also been done.

2,5-Diphenyl-1,3,4-thiadiazole has been isolated in low yield in the synthesis of 3,6-diphenyl-1,4-dihydro-1,2,4,5-tetrazine from sulfur, ethanol, hydrazine hydrate, and benzonitrile.

In the heteroaromatic series, it has been demonstrated that cyclopropyl conjugation is present in the highly interesting 3,6-dicyclopropyl-1,2,4,5-tetrazine and, as anticipated, to a lesser extent, in 3,6-dicyclopropyl-pyridazine in both the ground and excited states.

Attempts at synthesizing the diaza analogs of tropone and the tropylium cation by standard methods met with no success. However, some interesting rearrangements and new compounds were observed.

CHAPTER I

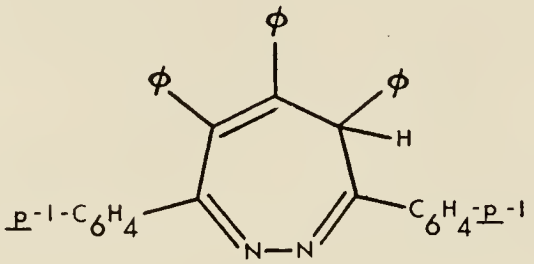
THE DIAZANORCARADIENE-DIAZEPINE REARRANGEMENT

Results and Discussion

The first step taken in dissecting and analyzing the thermal conversion of 2 to 3 outlined in Scheme 1 was to determine the structure of compound 3. The structure of 3 was attacked using x-ray spectroscopy. It was decided to employ the heavy atom technique by reacting sym-triphenylcyclopropene with the then unknown 3,6-bis(4-iodophenyl)-1,2,4,5-tetrazine (17) at elevated temperatures to give directly 3 with two phenyl rings carrying iodine atoms.

Since classical methods of synthesizing 17 had failed previously,[6] the recently developed method of Abdel-Rahman et al.[10] was used to produce the yellow dihydroderivative of 17 which was then oxidized to the deep purple 17. Unfortunately, 17 was contaminated with what is tentatively identified as 2,5-bis(4-iodophenyl)-1,3,4-thiadiazole (18) (see Chapter III) which was very difficult to remove due to the gross insolubility of both 17 and 18. The thiadiazole 18 could be separated from 17 only by chromatography over basic alumina with boiling xylene which tended to completely decompose the tetrazine 17 unless it was rapidly eluted from the column.

Reaction of 17, either chromatographed or crude, with sym-triphenylcyclopropene in refluxing xylene gave the desired substituted 3 without isolation of the intermediate substituted 2. The x-ray analysis[11] of the iodine-substituted 3 showed that it has the 4H-diazepine structure 19.



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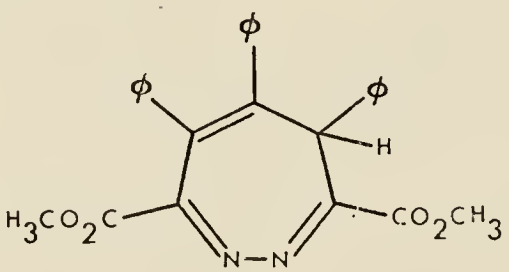
Obviously, the above described conversion of 10 to 11 should proceed in a manner analogous to the 2 to 3 conversion and product 11 should have the 4H-diazepine structure 20 rather than structure 12 as assigned by Sauer.



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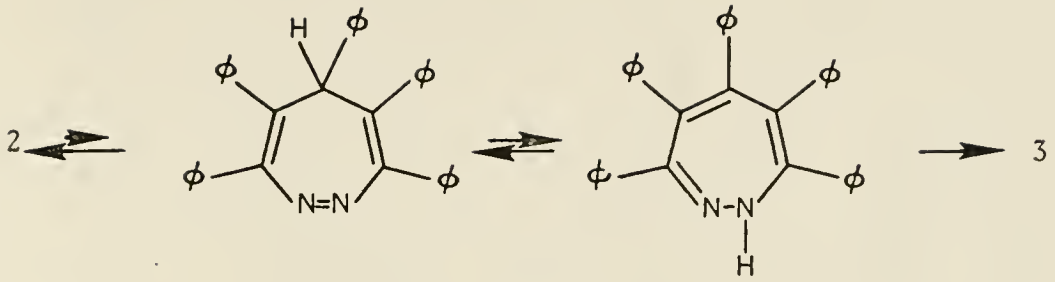
At least formally, the conversion of 2 to 3 may be considered as two concerted suprafacial 1,5-hydrogen shifts[12] from the open form of 2 as shown below in Scheme 4.



Scheme 4

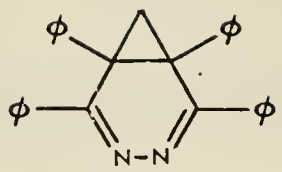
The kinetics of the thermal isomerization of 2 to 3 were followed by NMR at 150 and 140°. Good first-order kinetics were observed and the resulting kinetic parameters are given in Table I. The energy of activation (E_a) was found to be 33.4 kcal/mole. The kinetics indicated that the reaction is unimolecular and supported the mechanism of Scheme 4.

Table I

Kinetic Parameters for the Thermal Isomerization of 2 to 3

temp. (°C)	k (sec^{-1})	ΔH* (kcal/mole)	ΔS* (cal/mole-deg)
150.0	2.93×10^{-5}	32.6	-3.14
140.0	1.07×10^{-5}	32.6	-3.24

Taking the premise that two concerted 1,5-hydrogen shifts were responsible for the conversion of 2 to 3, it appeared of considerable mechanistic interest to examine some systems in which the cyclopropane ring of the diazanorcaradiene does not carry three phenyl rings as in 2. Two such systems are 21 and 22, which are simply 2 and 10 without a phenyl on the methylene carbon (C-7).



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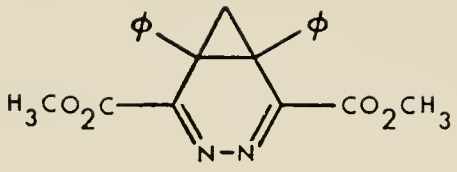


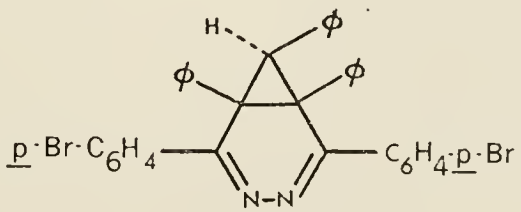
22

Both 21 and 22 are readily synthesized by the cycloaddition of 1,2-diphenylcyclopropene[13] with 1 and 9 respectively. The resulting adducts are bright yellow crystalline compounds whose spectral and analytical properties define their structure as that of the norcaradiene valence tautomer.

The aromatic region of the NMR spectrum of 21 shows two multiplets centered at τ2.18 and 2.80 integrating in the ratio 4:6 and a spike at 3.16 which accounts for ten protons. The lower field aromatic multiplet is assigned to the ortho protons of the phenyl rings attached to the azine linkage. Deshielding of these ortho protons by the electron-withdrawing and diamagnetically deshielding azine linkage is assumed. The higher field multiplet is assigned to the further removed meta and para protons of the phenyls at C-2 and C-4. The ten-proton spike which is at higher field than either multiplet accounts for the phenyls attached to the cyclopropane ring. The two methylene (C-7) protons, which are especially important for structural identification, appear as two widely separated

sharp doublets at τ6.31 (J = 5.5 Hz) and 8.68 (J = 5.5 Hz). That the methylene protons appear as two doublets could be accounted for by a diazacycloheptatriene which is frozen in a non-inverting conformation, but the chemical shift of both protons is more indicative of cyclopropyl than allylic protons. The higher field doublet is assigned to the endo proton which is shielded to some extent by the azine linkage. The lower field doublet is assigned to the exo proton which is deshielded by the phenyl rings attached to the cyclopropyl ring (vide infra).

At about this time preliminary x-ray crystallographic results by Fritchie[14] revealed that 23 indeed exists in the diazanorcaradiene form rather than the diazacycloheptatriene form. A notable result of Fritchie's investigation of 23 was that the cyclopropyl hydrogen occupies the exo position and lies in the deshielding region of the phenyls at C-1 and C-6. Thus, in assigning only non-aromatic proton as allylic rather than cyclopropyl on the basis of chemical shift, Battiste[2] was in error due to unforeseen diamagnetic deshielding effects.



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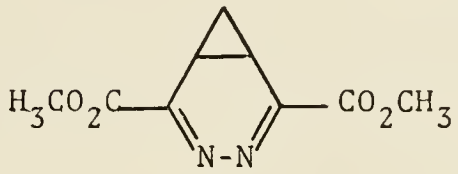
Heating 21 in pyridine caused noticeable broadening of the NMR doublets at temperatures as low as about 90°. The signals for both methylene protons completely disappeared at 150°. Although time-averaging of the two methylene protons was apparently occurring *via* ring inversion, no time-averaged singlet for a rapidly inverting diazanorcaradiene could ever be observed presumably due to decomposition (*vide infra*). Also, no signal for rearranged 21 could be found.

On heating to as high as about 190° in either d_5-nitrobenzene or napthalene, decomposition of 21 to an unidentified red oil was observed. Further heating converted the red oil to a yellow oil which could not be identified after chromatography and spectral analysis.

Compound 22 showed temperature-dependent NMR behavior similar to that exhibited by other diazanorcaradienes, such as 24, with ester groups in the 2- and 5-positions.[15] At -3.5° the molecule is frozen in a non-exchanging form which shows the expected NMR spectrum for the diazanorcaradiene structure. The phenyls attached to the cyclopropane ring show the expected ten-proton spike at τ2.95. The ester methyls, which are magnetically equivalent, appear as a singlet at τ6.35. Again, as in the NMR spectrum of 21, the cyclopropyl protons show up as two widely separated doublets at τ6.37 (J = 5.7 Hz) and 9.0 (J = 5.7 Hz). Warming the NMR solution of 22 to 37° causes complete disappearance of the cyclopropyl signals. The cyclopropyl doublets

coalesce at about 24° which is indicative of the phenyls actually inhibiting the opening of the diazanorcaradiene to the 5H-diazepine as the system 24 reported by Binsch and Sauer[15] coalesces at between 5 and 16°.



24

An attempt at thermally isomerizing 22 in refluxing dioxane only produced small amounts of what is assumed to be dimethyl 1,6-diphenyl-3,4-diazabicyclo[4.1.0]hept-2-en-5-ol-2,5-dicarboxylate (25) mainly on the basis of its NMR spectrum.

The NMR spectrum of 25 shows the expected broad singlet at τ1.15 for the N-H proton, two multiplets centered at 2.95 and 3.6 integrating 8:2 for the ten aromatic protons, a broad singlet for hydroxyl proton at 4.75, sharp singlets at 5.58 and 6.18 for the nonequivalent methyl protons, and an AB-quartet centered at 6.78 (J = 12.5 Hz) for the cyclopropyl protons.

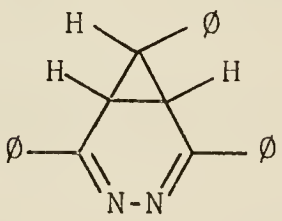
No attempt was made at assigning the stereochemistry of 25. The mass spectrum of 25 gives the correct molecular weight (364) but the cracking pattern in no way resembles the mass spectral cracking pattern produced by the precursor 22. In the mass spectrometer one might have expected the parent ion of 25 to lose a molecule of water to yield the

parent ion of 22, but apparently other processes are competitive with loss of water and, hence, the cracking pattern of 25 does not resemble that of 22. The addition of water across the carbon-nitrogen double bond of diazanorcaradienes is well-documented.[5,16] An attempt at an authentic synthesis of 25 was apparently a failure for unknown reasons.

Since of the two systems, 21 and 22, 22 should have shown the greater propensity for rearrangement[6] but did not rearrange, no attempt other than the high temperature NMR work was made at thermally isomerizing 21.

The thermal behavior of the simplest diazanorcaradiene, 6, which is 2 with no phenyls on the cyclopropyl carbons, was also investigated. Refluxing 6 in xylene for 18 hours produced nothing but tar and starting material.

Another system, 2,5,7-triphenyl-3,4-diazabicyclo[4.1.0] hepta-2,4-diene (7), was examined. Refluxing in dioxane for 132 hours yielded nothing but unidentifiable resin.



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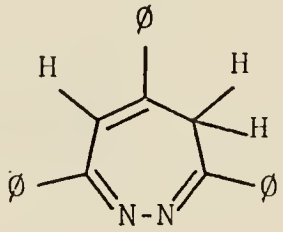
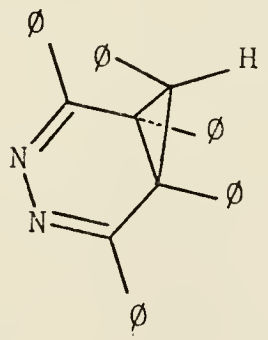


26

If 7 had rearranged to a 4H-diazepine via two concerted 1,5-hydrogen shifts, it would have rearranged to the known 26.[17] Diazepine 26 was found to be stable under the conditions used in the attempted rearrangement of 7.

From the above results it was concluded that three phenyls on the cyclopropane ring were necessary before a diazanorcaradiene will rearrange to a 4H-diazepine. However, it was still a mystery as to why systems 6, 7, 21, and 22 did not rearrange to at least some small extent if the rearrangement was taking place by way of a hydrogen shift mechanism.

Upon closer examination of the systems which do rearrange and those which do not, it was noted that in the systems which rearrange there is a phenyl ring over the azine linkage. Thus, 2 is 1,2,5,6-tetraphenyl-*endo*-7-phenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene as shown in structure 27. The compound 7 has the requisite phenyl in the 7-position, but this phenyl is *exo* to the azine linkage as shown in structure 28 since, in the absence of steric interaction from substituents in the 1- and 6-positions, the phenyl at C-7 prefers the *exo* position.



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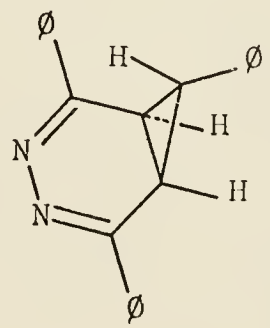

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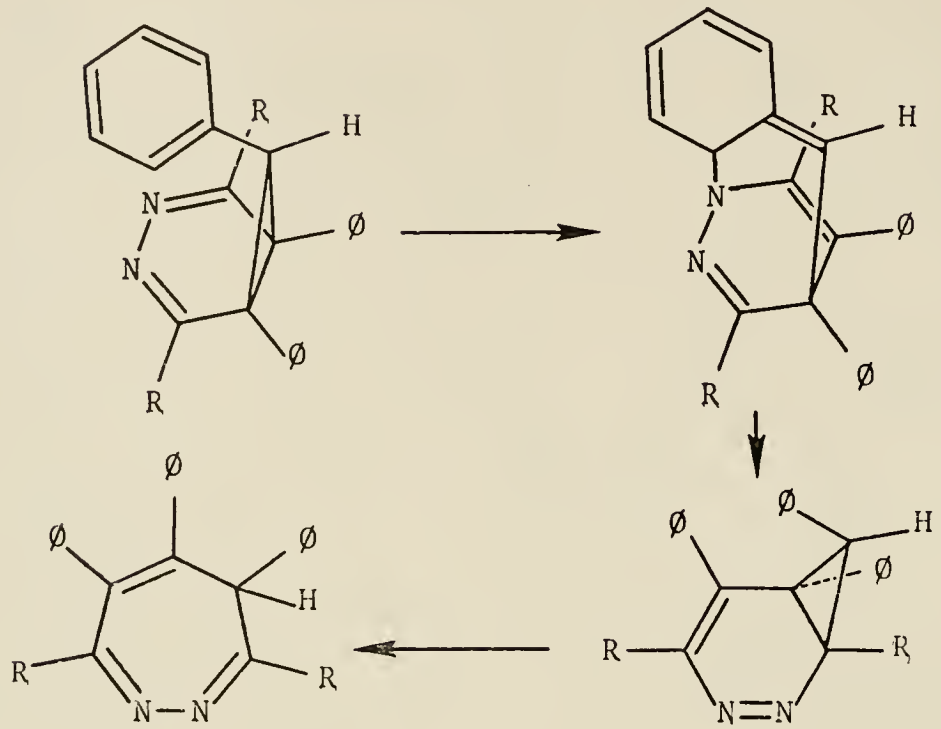
The above observations led to the hypothesis that perhaps the rearrangement is of the Cope ([3,3] sigmatropic)

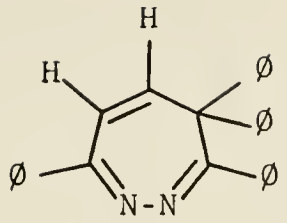
type involving the endo-7-phenyl as illustrated in Scheme 5.



Scheme 5

To test the idea of the Cope mechanism, the synthesis of 2,5,7,7-tetraphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (29) was attempted since this system would have the requisite endo-7-phenyl but no phenyls in the 1- and 6-positions. Rearrangement of 29 by the pathway depicted in Scheme 5 would lead to the diazepine 30.

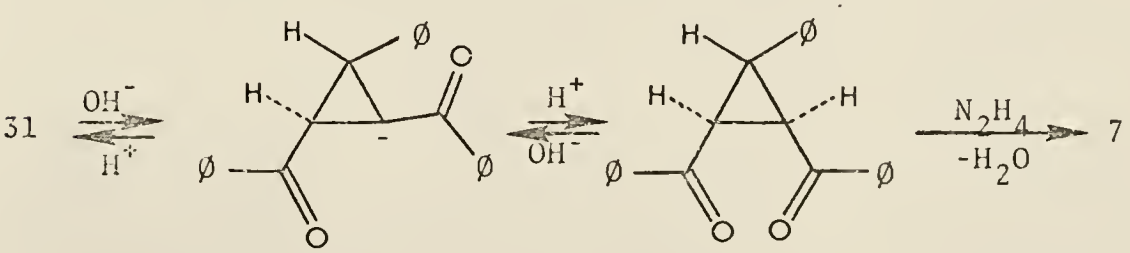
The NMR spectrum of 30 should show an aromatic multiplet with the previously described deshielding of the ortho protons of the phenyl at C-7. The ortho protons of the phenyl at C-3 probably would not show any deshielding as the phenyls at C-4 would impose steric restrictions forcing the C-3 phenyl out of the plane of the azine linkage. The



30

vinylic protons should appear as an AB-quartet. The mass spectrum of 30 should also be similar to that for 29 with loss of benzonitrile as the base peak (see Chapter II).

During their investigation of the diazanorcaradiene 7, Amiet and Johns[4] reported that 7 could be synthesized in low yield (7%) from trans-1,2-dibenzoyl-3-phenylcyclopropane (31) only by heating with hydrazine in ethanol for long periods of time, whereas the cis isomer of 31 reacted rapidly and almost quantitatively at room temperature. In the present investigation it was found that 7 could be produced in satisfactory yield (55.1%) from 31 at room temperature if a catalytic amount of sodium hydroxide was added to the mixture of 31 and hydrazine in ethanol. Presumably, the observed increase in yield is due to a rapidly established base-catalyzed cis-trans equilibration as shown in Scheme 6.



Scheme 6

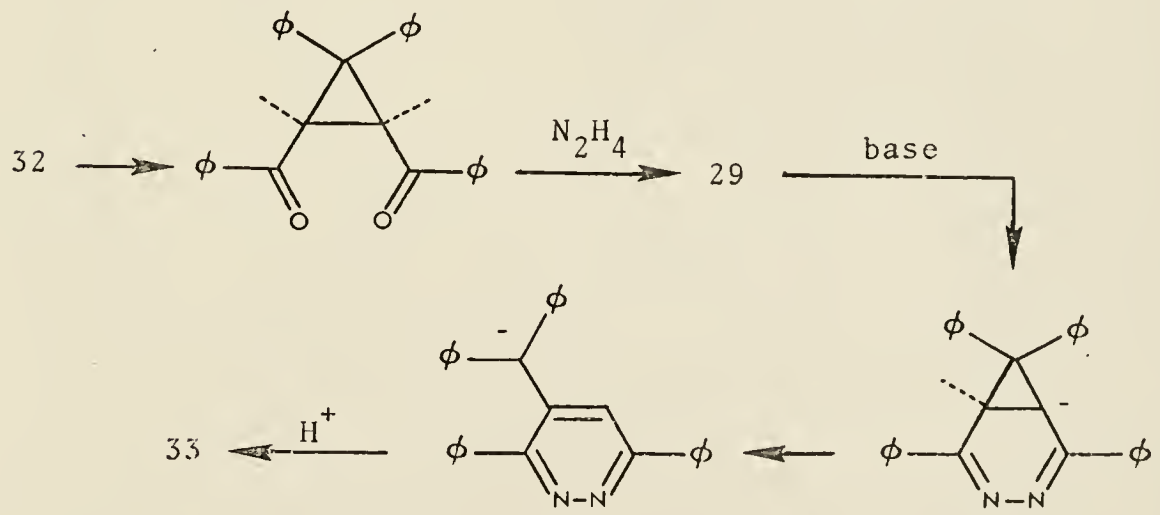
In view of the above observation, the synthesis of 29 was attempted by reaction of the known trans-1,2-dibenzoyl-3,3-diphenylcyclopropane (32)[18] with hydrazine in the presence of sodium hydroxide in ethanol. At room temperature in ethanol, 32 and hydrazine in the presence of sodium hydroxide showed no signs of reaction, i.e. no yellow color or precipitate. On refluxing, the reaction mixture developed a yellow coloration but then turned colorless again. The colorless crystals isolated from the reaction mixture at this point were not the desired 29, but an isomer $C_{29}H_{22}N_2$ as determined from the mass spectrum and elemental analysis.

In the aromatic region, the NMR spectrum of this isomeric compound 33 showed a multiplet centered at τ2.01 accounting for two protons and a multiplet at 2.8 accounting for nineteen protons indicating only one phenyl with ortho protons deshielded by an azine or otherwise electron-withdrawing group. The only other feature of the spectrum was a slightly broadened singlet at τ4.31. Mostly on the basis of the above NMR evidence the compound was identified as 3,6-diphenyl-4-benzhydrylpyridazine (33).

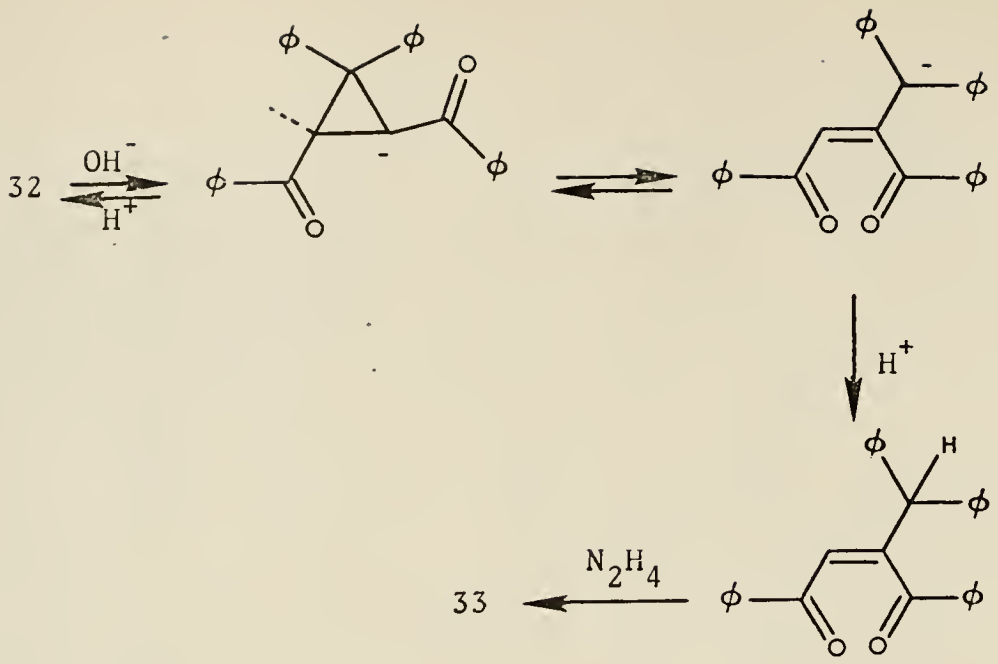
The phenyl in the 6-position is relatively free to assume coplanarity with the pyridazine ring, thus accounting for the pair of deshielded ortho protons. However, the phenyl in the 3-position is sterically crowded by the bulky benzhydryl group in the 4-position which inhibits coplanarity with the pyridazine ring and, thus, all five protons of the 3-phenyl are at approximately the same chemical

shift. The lone pyridazine ring proton is assumed to be masked by the higher field multiplet. The singlet at τ4.31 is accounted for by the benzhydryl proton. The fact that in the mass spectrum of 33 the parent ion is base peak is in accord with a pyridazine carrying aromatic substituents.

Due to the development of a transient yellow color during the formation of 33, it was not clear whether 29 is initially formed and then converted into 33 under the influence of base (Scheme 7) or 32 was transformed *via* a base-catalyzed ring-opening reaction into 2-benzhydryl-1,4-diphenylbut-*cis*-2-ene-1,4-dione which would then react with hydrazine to form 33 (Scheme 8).



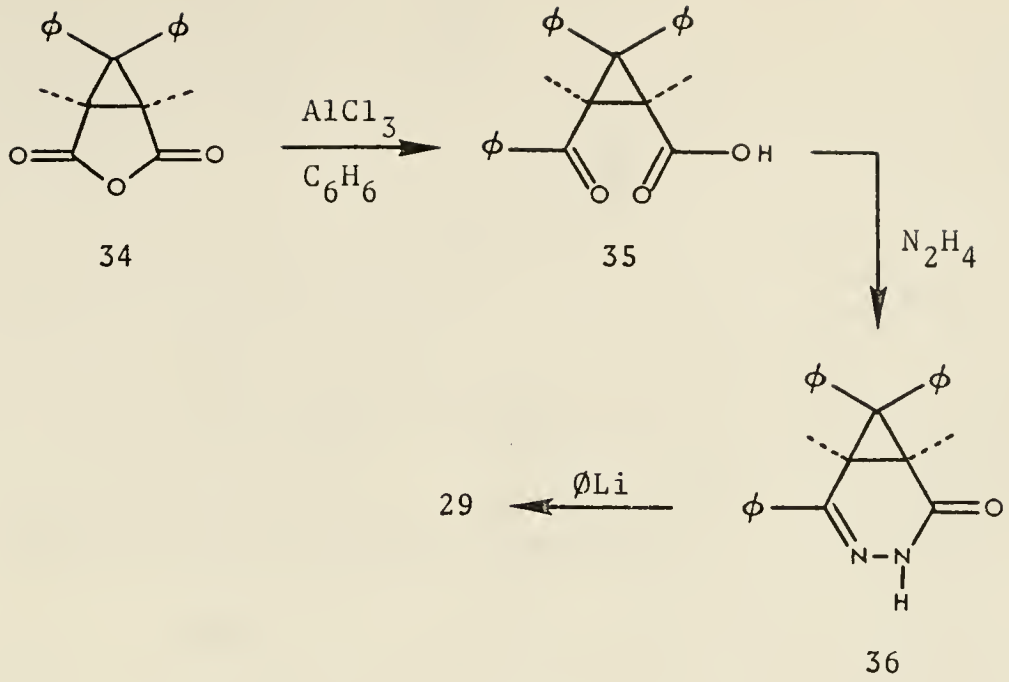
Scheme 7



Scheme 8

When 29 was finally synthesized at a later date, it was found to be insensitive to refluxing ethanolic sodium hydroxide in the time interval necessary for the formation of 33. Thus, it appears that a pathway similar to that in Scheme 8 is in operation in the formation of 33 from 32.

The failure to obtain 29 by the simple route above forced the adoption of a more elaborate synthetic scheme. The scheme chosen was similar to that developed by Maier[3] and is outlined below (Scheme 9) for this particular system.



Scheme 9

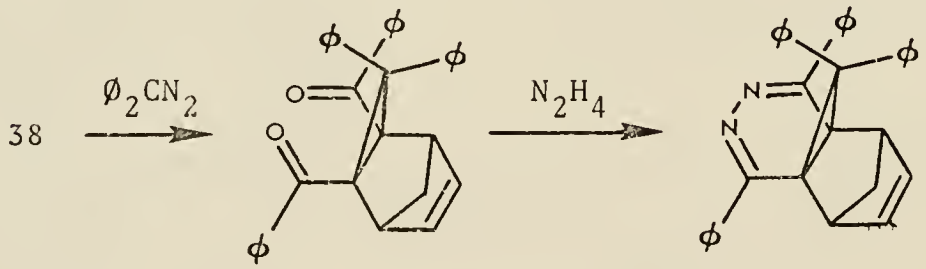
The known 34[18] was synthesized in good yield (61%) from diphenyldiazomethane[19] and commercial maleic anhydride simply by mixing the two reactants in benzene. The literature method[18,20] calls for mixing the two components and refluxing in benzene.

Presumably due to polymerization, treatment of a benzene solution of 34 with anhydrous aluminum chloride only resulted in the formation of yellow, aqueous bicarbonate soluble resin.

Addition of a benzene solution of 34 to anhydrous aluminum chloride in benzene yielded 77.7% of a compound tentatively identified as 3,3-diphenyl-trans-2-benzoylcyclopropanecarboxylic acid (37). Although the compound did not give a correct elemental analysis, it did give a correct mass spectral molecular weight (342) and, while the compound

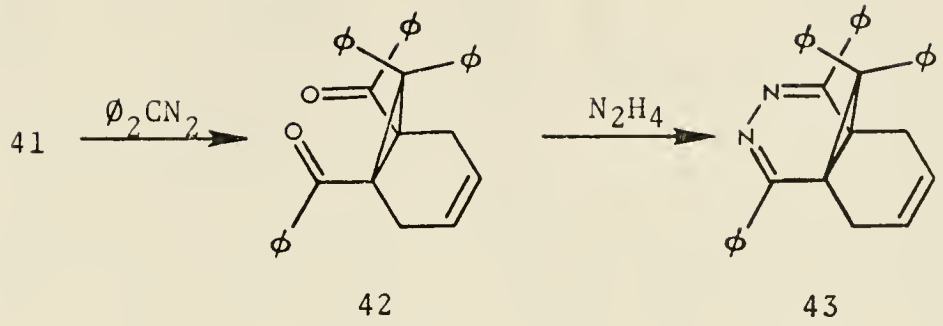
was fairly insoluble, it gave an NMR spectrum which showed only aromatic protons and an AB-quartet centered at τ6.06. The approximate coupling constant of 6 Hz for the AB-quartet suggested the trans assignment for 37.[21] When 29 was subsequently obtained, its AB-quartet for the cyclopropyl protons showed a coupling constant of 8.0 Hz which is indicative of a cis configuration.[21]

While the synthesis of 29 was in progress, a companion effort was directed towards the synthesis of more complicated, but just as physically useful systems such as 40 and 43. At first these systems appeared to be more readily accessible than 29. The proposed synthetic routes are outlined below in Schemes 10 and 11. The requisite 2,3-dibenzoylbicyclo[2.2.1]hepta-2,5-diene (38)[22] and 1,2-dibenzoylcyclohexa-1,4-diene (41)[23] were known and easily obtained on the multigram scale.



39 40

Scheme 10

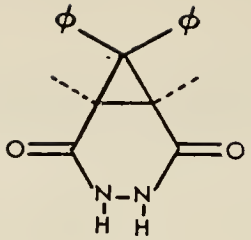


42 43

Scheme 11

Unfortunately, both 38 and 41 were very unreactive towards diphenyldiazomethane. On stirring for 24 days, 38 decolorized a solution of diphenyldiazomethane but workup of the colorless material caused decomposition to a purple substance which further decomposed to brown tar. Refluxing 41 in benzene with a large excess of diphenyldiazomethane gave rise to copious amounts of a material which is assumed to be benzophenone azine. Presumably the low reactivity of 38 and 41 towards diphenyldiazomethane is due to the cis arrangement of the benzoyl groups on the double bond in both cases. This factor has been noted previously.[24]

In an effort to bypass the critical synthetic intermediates 35 and 36 of Scheme 9, an attempt was made at the synthesis of 44 which, it was hoped, would add two moles of phenyllithium to produce 29.

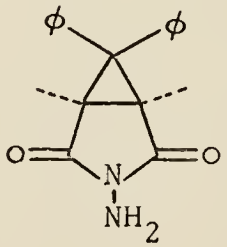


44

On treatment with hydrazine 3,3-diphenyl-cis-cyclopropanedicarboxylic acid[18] (45) was found to yield only water-soluble material which, on addition of mineral acid, regenerated 45. Presumably the water-soluble material is the hydrazine salt of the acid rather than the hydrazide or the desired 44.

Attempted addition of diphenyldiazomethane to maleic hydrazide[25] gave no identifiable products.

On refluxing the anhydride 34 with hydrazine in ethanol for 60 hours, a new crystalline substance is produced. The NMR spectrum, mass spectrum, and elemental analysis agreed with structure 44 but, unfortunately, the spectra also agreed with structure 46. The infrared, which shows a doublet rather than a singlet in the N-H stretch region, indicates that structure 46 is probably the better choice.



46

Cyclic bisamide 44 or its isomer 46 gave no identifiable products on attempted addition of phenyllithium under a variety of conditions.

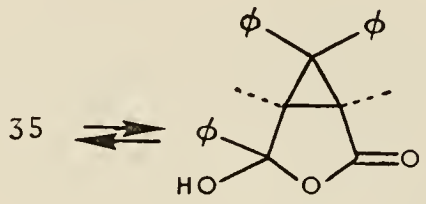
As a last resort, addition of phenylmagnesium bromide to the anhydride 34 was attempted with success. Equimolar quantities of the Grignard reagent and 34 produced 35 in low yield (6.9%) when the reaction was carried out at room temperature. Slightly better yields and cleaner product were obtained either by adding the Grignard reagent to 34 in toluene at dry ice temperatures or by use of the diphenylcadmium reagent.

Besides giving the correct molecular weight and elemental analysis, the ketoacid 35 gave the expected NMR spectrum. In the aromatic region, there is a low-field multiplet centered at τ1.9 integrating for two protons and a higher-field multiplet centered at 2.6 integrating for thirteen protons. The τ1.9 multiplet is assumed to be due to the ortho protons of the benzoyl phenyl. The τ2.6 multiplet accounts for the remaining aromatic protons. The expected AB-quartet at τ6.48 integrates for two protons. The coupling constant of 8.0 Hz is that to be expected for cis protons on a cyclopropyl ring of this sort.[21] Ketoacid 35 also shows a carboxylic acid proton as a very broad, almost undetectable singlet at about τ-1.4.

The infrared (KBr pellet) of 35 shows no strong absorbance for hydroxyl as would be expected for a carboxylic acid hydroxyl. The carbonyl stretch of 35 is at 1730 cm^{-1} which

is more typical of a lactone than a free carboxylic acid. The above is in accord with the observation that ketoacids similar[3] to 35 usually exist exclusively in a pseudo acid form (structure 47) in the solid state.

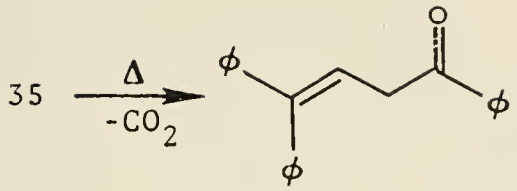
In solution, ketoacids such as 35 tend to form an equilibrium between free acid and psuedo acid.[3]



47

On melting, 35 evolves carbon dioxide to yield some tar and the known 1,4,4-triphenylbut-3-en-1-one (48).[26] The melting point and infrared carbonyl absorption were in close agreement with that reported.[26]

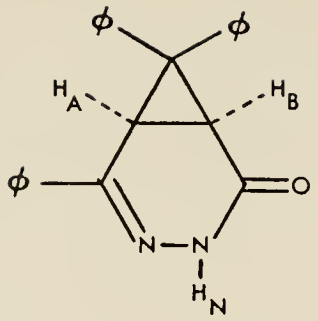
The previously unreported NMR spectrum for 48 fits the compound well. The aromatic region shows a two-proton multiplet centered at τ2.17 and a thirteen-proton multiplet centered at 2.7. As with 35 (vide supra), the two aromatic multiplets respectively account for the ortho protons of the phenyl attached to the carbonyl and the remaining aromatic protons. The remaining portion of the spectrum shows the expected vinylic triplet at τ3.59 (J = 7.0 Hz) integrating for one proton and the expected methylene doublet at 6.21 (J = 7.0 Hz) integrating for two protons.



48

Stirring a solution of 35 and hydrazine hydrate in ethanol for 24 hours gave the desired 2,7,7-triphenyl-5-keto-3,4-diazabicyclo[4.1.0]hept-2-ene (36) as a white crystalline precipitate. Even though 36 gave a correct mass spectral molecular weight (338), an acceptable elemental analysis could not be obtained. The analysis suggested the presence of a half mole of water of crystallization. The infrared spectrum showed the expected carbonyl stretch[3] at 1670 cm^{-1}.

Although fairly insoluble, an NMR spectrum of 36 could be obtained. The amide proton appeared as a broad absorbance at τ1.9. As expected, the ortho protons of the phenyl ring attached to the carbon-nitrogen double bond appeared as a distinct multiplet at about τ2.0, with the remaining aromatic protons appearing at higher field (2.40 - 3.16). The two cyclopropyl protons appeared as the expected AB-quartet at τ6.88 (J_{AB} = 8.0 Hz). The upfield half of the quartet is split again into a pair of doublets by coupling with the amide proton (H_N) (J_{BN} = .1.5 Hz, J_{AN} = 0.0 Hz).



36

The coupling between H_B and H_N finds precedent in the literature[27] and is not unexpected, especially when, upon examination of a molecular model of 36, it is found that H_B and H_N fit nicely into the well-known "W" pattern.[28] There is no coupling between H_A and H_N as determined from an HA-100 spectrum.

Addition of phenyllithium to 36 proceeded smoothly producing 29 in moderate yield (47.2%). Diazanorcaradiene 29 analyzed correctly and gave a correct mass spectral molecular weight (398) in addition to a reasonable fragmentation pattern.

In the aromatic region, the NMR spectrum of 29 displayed a four-proton multiplet centered at τ1.8, a six-proton multiplet centered at 2.5, and two five-proton singlets at 2.71 and 3.03. Presumably the lower field multiplet is due to the ortho protons of the phenyls on the deshielding azine linkage while the higher field multiplet again accounts for the remaining protons on the 2- and 4-phenyls. It is assumed that the higher field

aromatic singlet is due to the cyclopropyl phenyl over the slightly shielding region of the azine linkage while the lower field aromatic singlet is due to the other unshielded cyclopropyl phenyl. The only other feature of the NMR spectrum of 29 is a sharp singlet at τ6.58 integrating for two protons. The singlet is due to the now equivalent cyclopropyl protons.

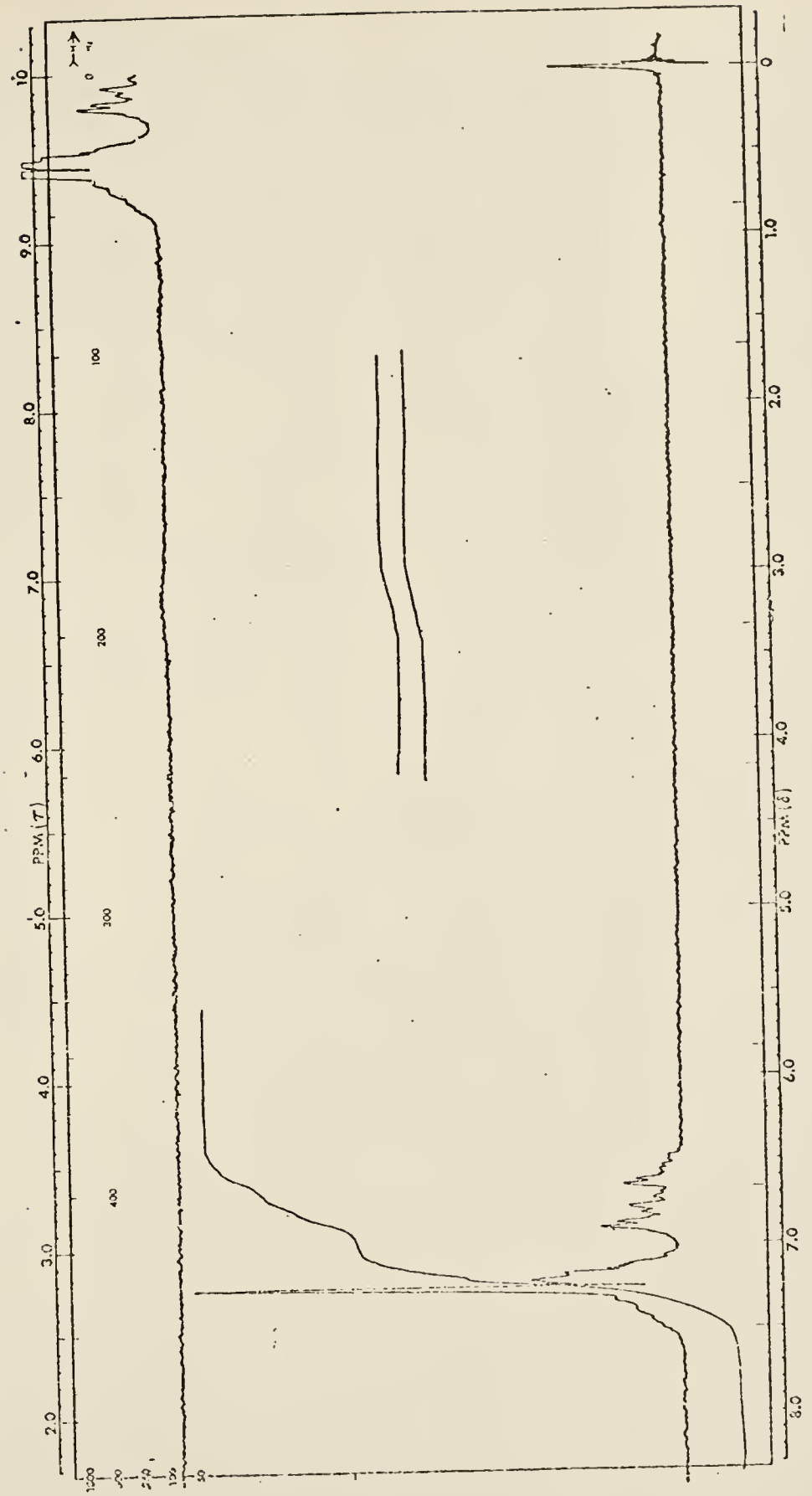
Chemical evidence for structure 29 was provided by its acid-catalyzed conversion into pyridazine 33 which had been previously characterized.

In refluxing xylene over a 24-hour period, 29 gives rise to a new, colorless, unknown isomer 49 which does not show the properties usually exhibited by 4H-diazepines even though it analyzes correctly and gives the correct molecular weight of 398.

The mass spectrum of 49 is completely different from that of 29. The parent ion is base peak rather than the parent minus benzonitrile ion which is only 3.5% of base peak. The mass spectrum of 49 is quite featureless except for peaks at 397 (21%) and 321 (14%).

The NMR spectrum of 49 is also quite featureless displaying, as illustrated in Figure 1, only N-H at τ0.18 and aromatic multiplets centered at 2.7 and 3.2. The three NMR signals integrated for one, fifteen, and six protons respectively. That the signal at τ0.18 is due to hydrogen attached to nitrogen was proved by deuterium exchange with heavy water which readily destroyed this signal.

Figure 1. NMR spectrum of unknown 49 in $CDCl_3$

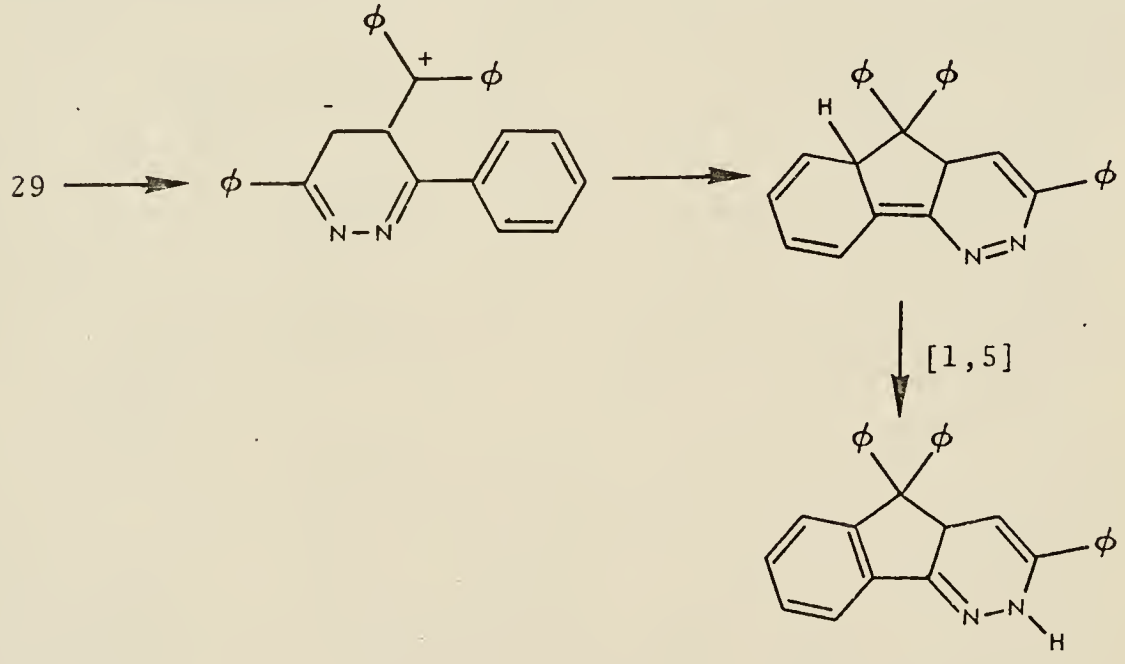

PPM (τ)
PPM (δ)
10
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
100
200
300
400

Changing the NMR solvent from deuteriochloroform to d_5-pyridine altered the spectrum drastically as shown in Figure 2, but gave no new information. Unchanged 49 could be recovered after dissolution in pyridine.

Infrared and UV spectra gave no further useful information as to the identity of 49.

It was fairly obvious that 49 was not the desired 4H-diazepine 30. The possibilities left for 49 were all $C_{29}H_{22}N_2$ isomers which would show the observed spectroscopic properties of 49 and have a reasonable mechanistic route for their formation.

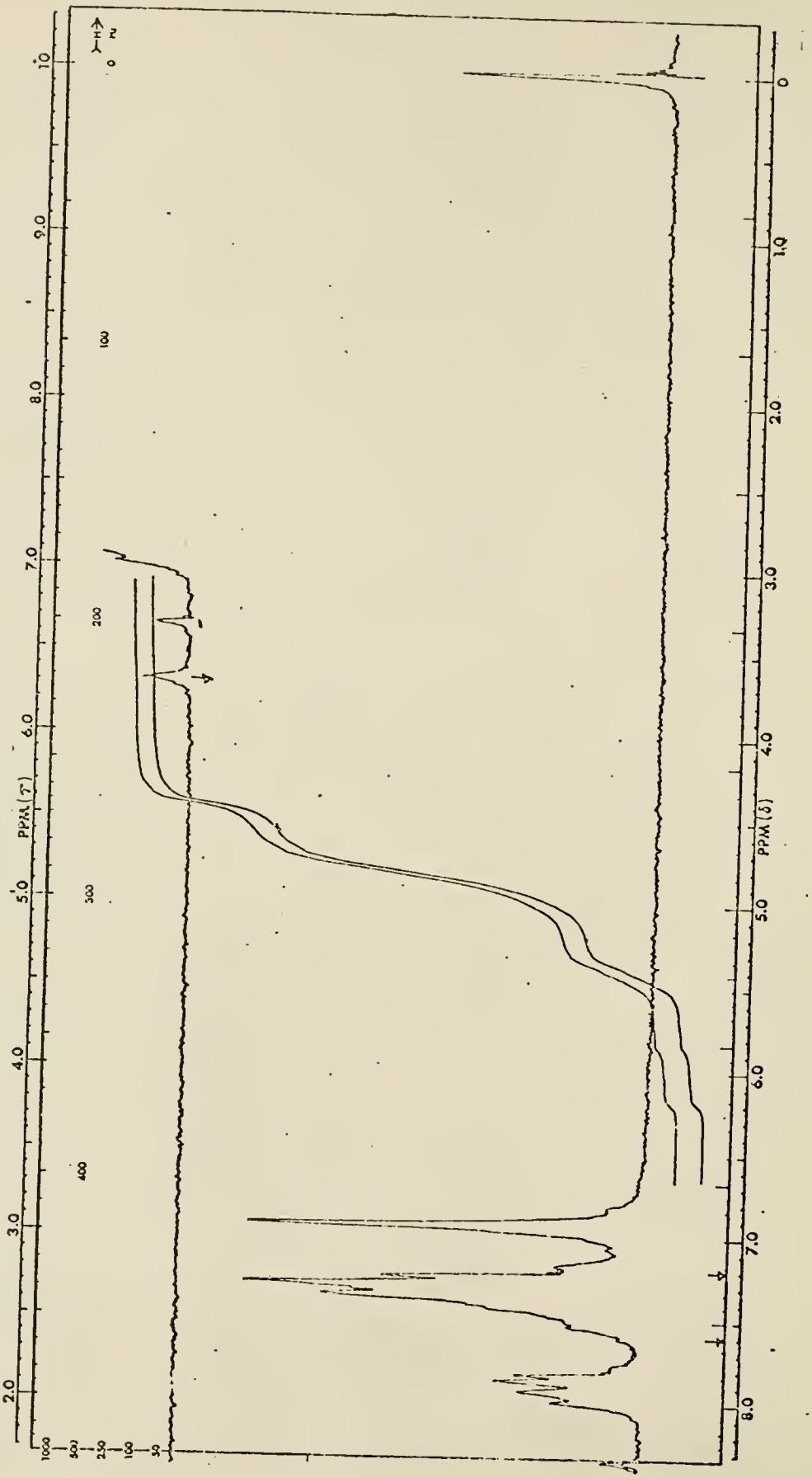
The first possibility chosen for 49 was structure 50 which is shown along with a possible mechanism (Scheme 12).



50

Scheme 12

Figure 2. NMR spectrum of unknown 49 in d_5-pyridine


PPM (τ)
PPM (δ)
100
200
300
400
1000
500
250
100
50

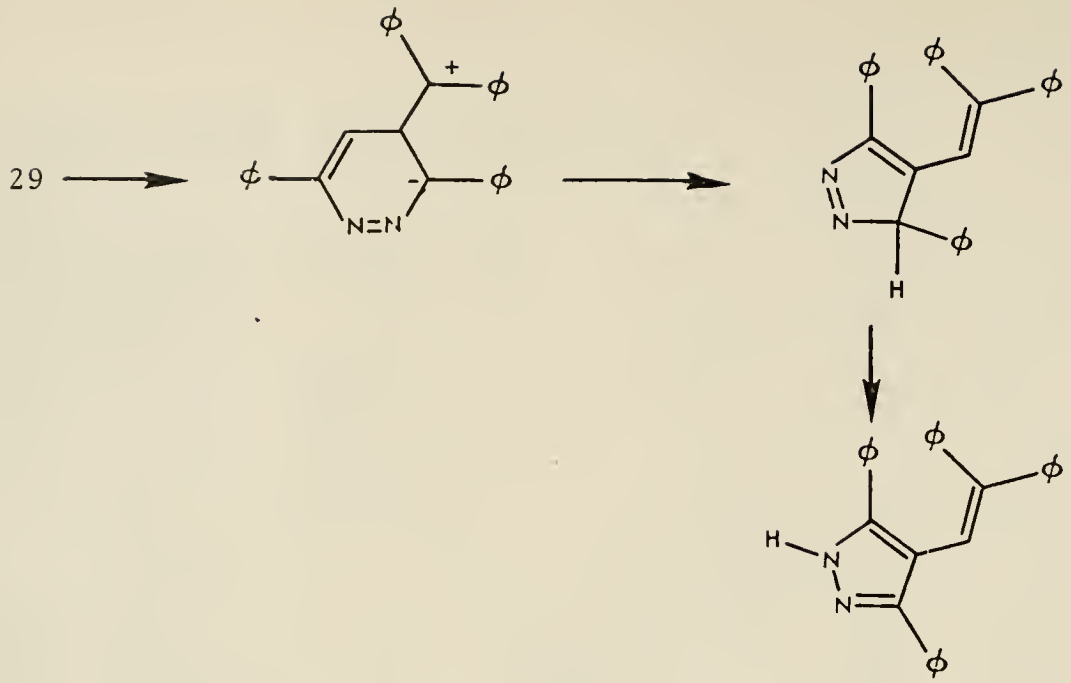
Structure 50 would fit the spectroscopic data if one assumes sufficient deshielding of the vinylic and aliphatic protons for them to appear in the aromatic region of the NMR. However, 50 is a dihydropyridazine and, on the basis of previous work,[29] should readily oxidize to the fully aromatic pyridazine.

Oxidation of 49 with potassium dichromate in aqueous acetic acid gave only some tar and a 41.3% recovery of starting material. Extensive chromatography produced no more material.

Oxidation of 49 with 1,2-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave only dark green, difficultly soluble material which, on chromatography over basic alumina, yielded 87% recovered starting material which showed no peak in the mass spectrum for 49 minus two hydrogens.

At this point it became fairly obvious that 49 does not possess a dihydropyridazine structure or any other structure which could be easily oxidized.

The next structure considered was structure 51 shown below in Scheme 13.

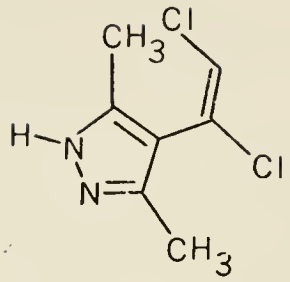


51

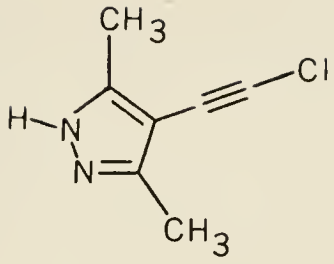
Scheme 13

There is no chemical evidence for or against 51. Once again one must assume sufficient deshielding of the vinylic proton to place it in the aromatic region in the NMR. Other spectroscopic data do not really speak for or against structure 51.

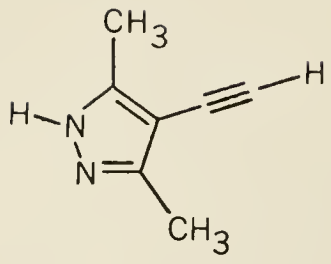
In the series 52, 53, and 54,[30] the proton on the pyrazole nitrogen appears in the NMR spectrum at δ13.3, 10, and 7.22 as a broad singlet whose position is concentration dependent. The position of the N-H proton of 49 is at about δ9.8.



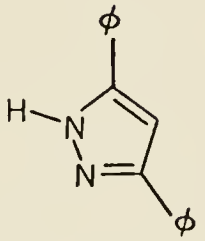
52



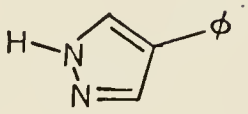
53



54



55



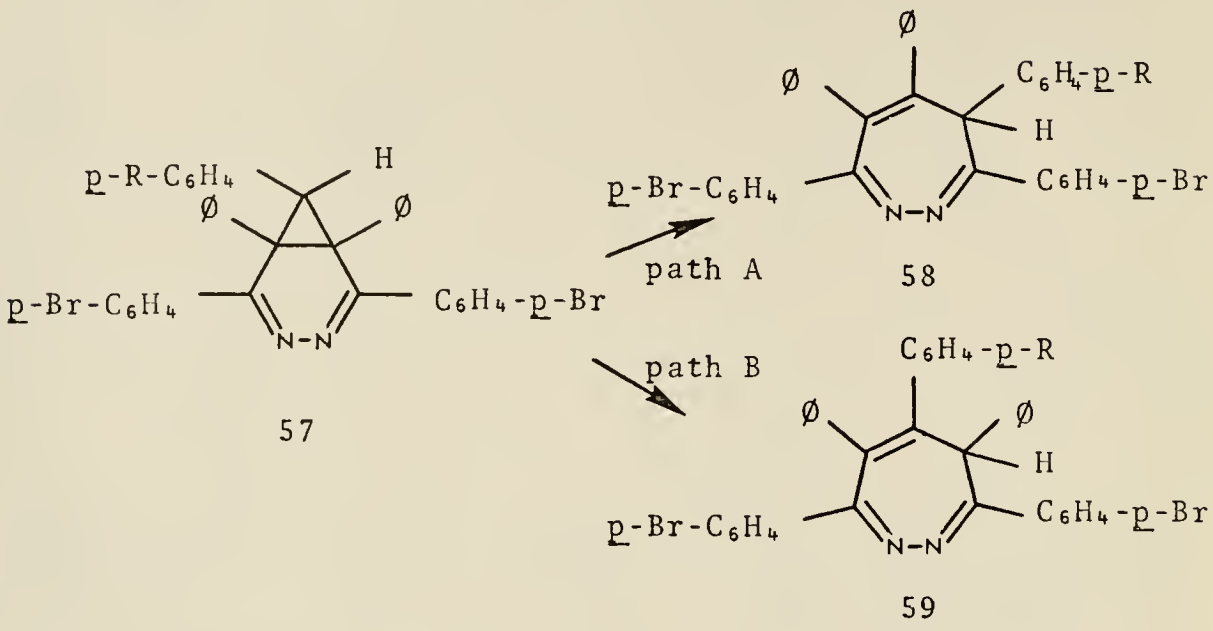
56

For the two compounds 55 and 56,[31] the UV spectra respectively consist of λ_{max} = 256 nm (ε = 33100) and λ_{max} = 250 nm (ε = 15100). The UV maximum of 49 is at 237 nm (ε = 28400) with inflections at 255 and 298 nm. Possibly, steric interactions among the two phenyls and the phenylstyryl group of 51 would cause a hypsochromic shift.

Since 49 was not the desired 4H-diazepine 30 and since 49 could not be identified, other means to determine the mechanism of the diazanorcaradiene-diazepine isomerization were sought.

The most direct and reasonable approach to this question involved resorting to a suitably labeled system which was known to rearrange and whose rearrangment product could be

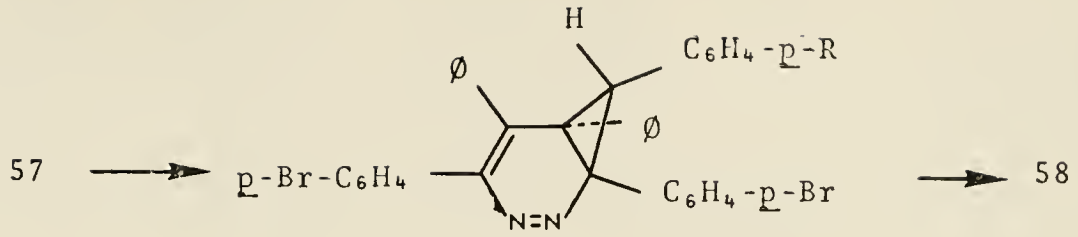
identified by x-ray methods. The diazanorcaradiene 57 was chosen as an appropriate system for study.



Scheme 14

As outlined in Scheme 14, the 4H-diazepine 59 would result if 57 underwent electrocyclic ring opening to the corresponding 5H-diazepine followed by two consecutive supra-facial concerted 1,5-hydrogen shifts (path B) as illustrated previously in Scheme 4 for diazanorcaradiene 2.

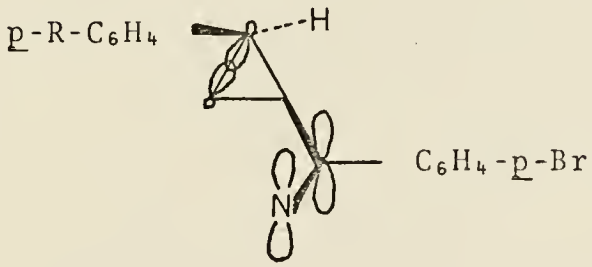
The diazepine 58 could arise in several ways. First, 58 could result from the Cope-type mechanism previously illustrated in Scheme 5 for the diazanorcaradiene 2. Also, 58 can arise by a Berson-Willcott Bones rearrangement[32] whereby C-7 of structure 57 "walks" around the six-membered ring to produce a 2,3-diazabicyclo[4.1.0]hepta-2,4-diene 60 which is unstable and opens up to the 4H-diazepine as depicted in Scheme 15.



60

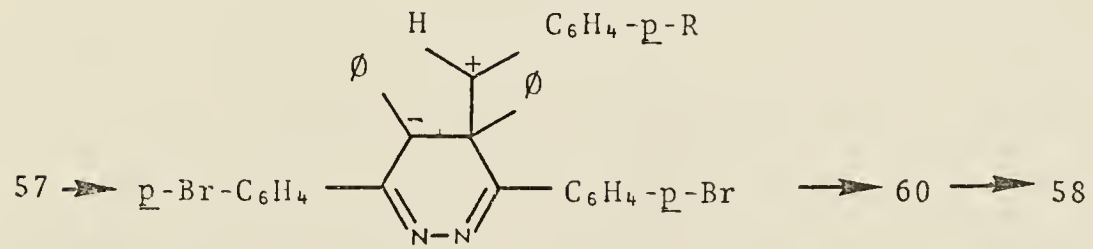
Scheme 15

The first step of Scheme 15 is concerted if the movement of C-7 occurs with retention at C-7 as shown in structure 61 since this is a [1,5] sigmatropic change.[12]



61

Other nonconcerted mechanisms similar to the Bones rearrangement may also be envisioned. One such mechanism involving a dipolar (or diradical) intermediate is given in Scheme 16.



Scheme 16

For the synthesis of 57, the problem reduces to the preparation of triphenylcyclopropene with only the 3-phenyl substituted with a group which can be observed by x-ray, e.g. halogen, small aliphatic groups, etc. The above means that no synthesis in which all three cyclopropenyl carbons become equivalent chemically is satisfactory. Thus, syntheses of sym-triphenylcyclopropene such as that developed by Battiste are unsatisfactory.[29]

Recently, it was demonstrated by Longone and Stehouwer[13] that hydride ion can be added to the known diphenylcyclopropenyl cation to give exclusively 1,2-diphenylcyclopropene in high yield. Thus, it was reasoned that an appropriately substituted phenylmagnesium bromide could be added to the same cation to give the desired substituted triphenylcyclopropene.

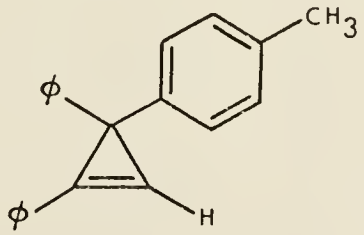
As a first attempt, p-chlorophenylmagnesium bromide was added to diphenylcyclopropenyl perchlorate to produce, after chromatography, a colorless solid whose NMR spectrum showed only a singlet at τ6.79 (sym-triphenylcyclopropene - τ6.8[33]) and an aromatic multiplet. However, the aromatic multiplet integrated much too high and the compound tended to discolor even in the absence of air and light. It was assumed that the desired 3-(4-chlorophenyl)-1,2-diphenylcyclopropene (62) had been obtained, but it could not be purified.

The same reaction as above was repeated with p-tolylmagnesium bromide. Good, clean product was obtained only if the cation was added to the solution of the Grignard reagent slowly. Rapid addition caused production of resinous

conglomerations which discolored the final product as in the case of cyclopropene 62.

The 3-(4-methylphenyl)-1,2-diphenylcyclopropene (63) characterized as expected. Besides giving a correct elemental analysis, 63 displayed the right mass spectral molecular weight (282). The NMR spectrum of 63 showed the expected aromatic multiplet centered at τ2.64 integrating for fourteen protons and two singlets at 6.83 and 7.76 integrating for one and three protons respectively. The τ6.83 signal is typical for a triphenylcyclopropene cyclopropenyl proton as was mentioned above. The τ7.76 signal is, of course, due to the methyl group.

If the Grignard reagent had added so as to give the isomeric cyclopropene 64, a one-proton singlet at ca. τ2.6[34] rather than 6.83 would have been anticipated.



64

The infrared spectrum of 63 displayed the typical cyclopropene carbon-carbon double bond stretch at 1830 cm^{-1} (sym-triphenylcyclopropene - 1820 cm^{-1} [34]). The UV spectrum of 63 was also very useful as it showed the maxima characteristic of a sym-triphenylcyclopropene at 332.5 nm

(ε = 23000), 315 nm (ε = 28000), 305 nm (s, ε = 22000), 302 nm (infl.), and 228 nm (ε = 32000). For comparison, the UV spectrum of sym-triphenylcyclopropene itself in ethanol consists of maxima at 330 nm (ε = 24200), 313 nm (ε = 29000), and 228 nm (ε = 30600).[35]

Cycloaddition of 63 with 3,6-bis(4-bromophenyl)-1,2,4,5-tetrazine (65)[6] produced the expected 2,5-bis-(4-bromophenyl)-7-(4-methylphenyl)-1,6-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (66). The diazanorcaradiene analyzed correctly and gave a correct mass spectral molecular weight (644). The diazanorcaradiene also gave a reasonable mass spectral fragmentation pattern which is discussed in Chapter II.

The NMR spectrum of 66 simply consisted of a twenty-two-proton aromatic multiplet centered at τ2.93, a one-proton singlet at 5.03 for the cyclopropyl proton, and a three-proton singlet at 7.83 for the methyl group. For comparison purposes, the cyclopropyl proton of the analogous diazanorcaradiene 2 appears at τ4.98.[2]

The thermal rearrangement of 66 in refluxing xylene proceeded more rapidly than was anticipated and, as a result, a much lower yield of the 4H-diazepine was obtained than was expected due to decomposition. Presumably, the methyl group of the substituted phenyl aids in the decomposition of the 4H-diazepine 67 to the corresponding pyrroles and benzonitriles. Diazepine 67 gave the anticipated analytical and spectral data as recorded in the Experimental Section (Chapter V).

Table II

Bond Distances and Their Estimated Standard Deviations in Diazepine 67

Atoms		Distance (Å)	e.s.d.[a]
Br(1)	C(E4)	1.91	0.01
C(E4)	C(E5)	1.38	0.01
C(E5)	C(E6)	1.40	0.01
C(E6)	C(E1)	1.37	0.01
C(E1)	C(E2)	1.39	0.01
C(E2)	C(E3)	1.38	0.01
C(E3)	C(E4)	1.37	0.01
C(E1)	C(5)	1.50	0.01
C(5)	N(1)	1.31	0.01
N(1)	N(2)	1.39	0.01
N(2)	C(1)	1.29	0.01
C(1)	C(A1)	1.47	0.01
C(A1)	C(A2)	1.40	0.01
C(A2)	C(A3)	1.38	0.01
C(A3)	C(A4)	1.37	0.01
C(A4)	Br(2)	1.91	0.01
C(A4)	C(A5)	1.36	0.01
C(A5)	C(A6)	1.41	0.01
C(A6)	C(A1)	1.39	0.01
C(1)	C(2)	1.52	0.01
C(2)	C(B1)	1.53	0.01
C(B1)	C(B2)	1.39	0.01
C(B2)	C(B3)	1.43	0.01
C(B3)	C(B4)	1.37	0.01
C(B4)	C(Me)	1.54	0.01
C(B4)	C(B5)	1.41	0.01
C(B5)	C(B6)	1.37	0.01
C(B6)	C(B1)	1.40	0.01
C(2)	C(3)	1.52	0.01
C(3)	C(C1)	1.50	0.01
C(C1)	C(C2)	1.40	0.01
C(C2)	C(C3)	1.41	0.01
C(C3)	C(C4)	1.38	0.01
C(C4)	C(C5)	1.36	0.01
C(C5)	C(C6)	1.42	0.01
C(C6)	C(C1)	1.38	0.01
C(3)	C(4)	1.34	0.01
C(4)	C(D1)	1.48	0.01
C(D1)	C(D2)	1.42	0.01
C(D2)	C(D3)	1.40	0.01
C(D3)	C(D4)	1.40	0.01
C(D4)	C(D5)	1.43	0.01
C(D5)	C(D6)	1.40	0.01
C(D6)	C(D1)	1.39	0.01
C(4)	C(5)	1.48	0.01

[a] estimated standard deviation.

Table III

Bond Angles and Their Estimated Standard Deviations in Diazepine 67

Atoms			Angle (deg.)	e.s.d.[a]
Br(1)	C(E4)	C(E5)	117.8	0.5
Br(1)	C(E4)	C(E3)	119.5	0.5
C(E4)	C(E5)	C(E6)	117.1	0.7
C(E5)	C(E6)	C(E1)	121.3	0.6
C(E6)	C(E1)	C(E2)	119.8	0.6
C(E1)	C(E2)	C(E3)	120.2	0.6
C(E2)	C(E3)	C(E4)	118.9	0.7
C(E3)	C(E4)	C(E5)	122.7	0.7
C(5)	C(E1)	C(E2)	118.6	0.6
C(5)	C(E1)	C(E6)	121.6	0.6
C(4)	C(5)	C(E1)	119.7	0.6
C(4)	C(5)	N(1)	125.7	0.6
N(1)	C(5)	C(E1)	114.5	0.6
C(5)	N(1)	N(2)	121.4	0.5
N(1)	N(2)	C(1)	121.3	0.5
N(2)	C(1)	C(A1)	115.9	0.6
N(2)	C(1)	C(2)	123.9	0.6
C(2)	C(1)	C(A1)	120.0	0.6
C(A1)	C(A2)	C(A3)	120.3	0.7
C(A2)	C(A3)	C(A4)	119.0	0.7
C(A3)	C(A4)	Br(2)	118.6	0.6
C(A3)	C(A4)	C(A5)	123.2	0.7
C(A5)	C(A4)	Br(2)	118.2	0.6
C(A4)	C(A5)	C(A6)	118.0	0.7
C(A5)	C(A6)	C(A1)	120.6	0.7
C(A6)	C(A1)	C(A2)	118.9	0.6
C(1)	C(A1)	C(A6)	119.2	0.6
C(1)	C(A1)	C(A2)	121.9	0.6
C(1)	C(2)	C(3)	102.8	0.5
C(1)	C(2)	C(B1)	115.7	0.6
C(3)	C(2)	C(B1)	116.0	0.6
C(B1)	C(B2)	C(B3)	121.1	0.7
C(B2)	C(B3)	C(B4)	119.0	0.7
C(B3)	C(B4)	C(Me)	121.2	0.7
C(Me)	C(B4)	C(B5)	119.1	0.7
C(B3)	C(B4)	C(B5)	119.7	0.7
C(B4)	C(B5)	C(B6)	121.4	0.7
C(B5)	C(B6)	C(B1)	120.0	0.7
C(B6)	C(B1)	C(B2)	118.9	0.6
C(2)	C(B1)	C(B2)	120.8	0.6
C(2)	C(B1)	C(B6)	119.9	0.6
C(2)	C(3)	C(C1)	116.8	0.6
C(2)	C(3)	C(4)	120.1	0.6
C(4)	C(3)	C(C1)	123.0	0.6

Table III (continued)

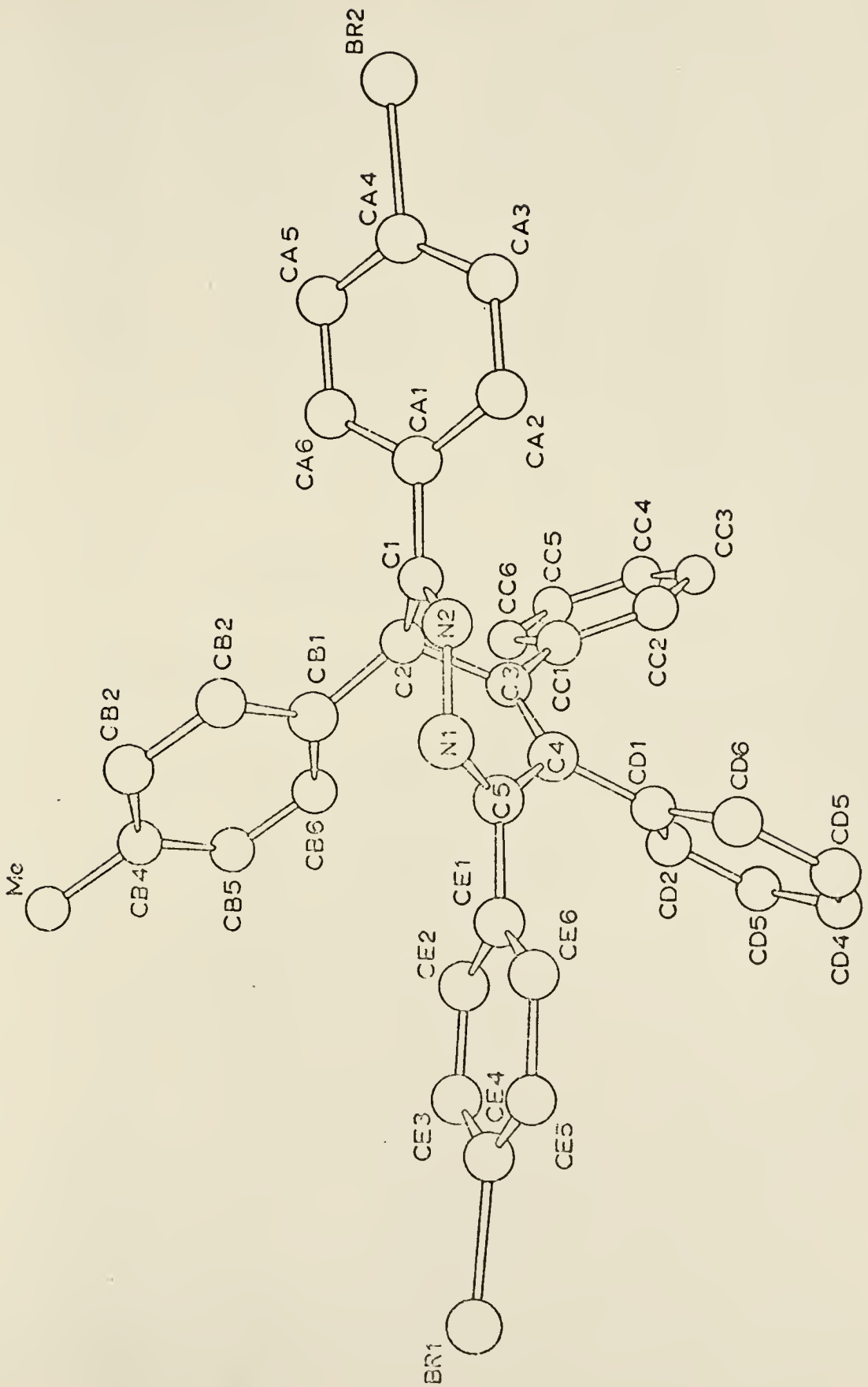
Atoms			Angle (deg.)	e.s.d.[a]
C(C1)	C(C2)	C(C3)	120.2	0.7
C(C2)	C(C3)	C(C4)	119.3	0.8
C(C3)	C(C4)	C(C5)	121.0	0.8
C(C4)	C(C5)	C(C6)	120.5	0.7
C(C5)	C(C6)	C(C1)	119.1	0.7
C(C6)	C(C1)	C(C2)	119.8	0.6
C(3)	C(C1)	C(C2)	120.3	0.6
C(3)	C(C1)	C(C6)	119.9	0.6
C(3)	C(4)	C(5)	120.7	0.6
C(5)	C(4)	C(D1)	114.0	0.5
C(3)	C(4)	C(D1)	125.3	0.6
C(4)	C(D1)	C(D2)	121.5	0.6
C(4)	C(D1)	C(D6)	120.7	0.6
C(D1)	C(D2)	C(D3)	121.5	0.7
C(D2)	C(D3)	C(D4)	118.8	0.7
C(D3)	C(D4)	C(D5)	121.3	0.8
C(D4)	C(D5)	C(D6)	117.8	0.7
C(D5)	C(D6)	C(D1)	122.9	0.7
C(D6)	C(D1)	C(D2)	117.7	0.6

[a]estimated standard deviation.

The x-ray analysis of 67, which is described in the Experimental Section, revealed that the rearrangement of 66 follows path A given in Scheme 14 above. An ORTEP-generated model of 67 is shown in Figure 3. A table of bond lengths is given in Table 2 and a table of bond angles is given in Table 3.

At this point, all that can be said in the absence of further data is that diazanorcaradienes containing one phenyl on each cyclopropyl position rearrange to 4H-diazepines by one of the mechanisms discussed above involving movement of an entire carbon rather than hydrogen shifts. Once again a system whose rearrangement appeared to be simple on the surface turned out to be quite complex on closer examination.

Figure 3. ORTEP-generated diagram of 3,7-bis(4-bromophenyl)-4-(4-methylphenyl)-5,6-diphenyl-4H-1,2-diazepine (67)

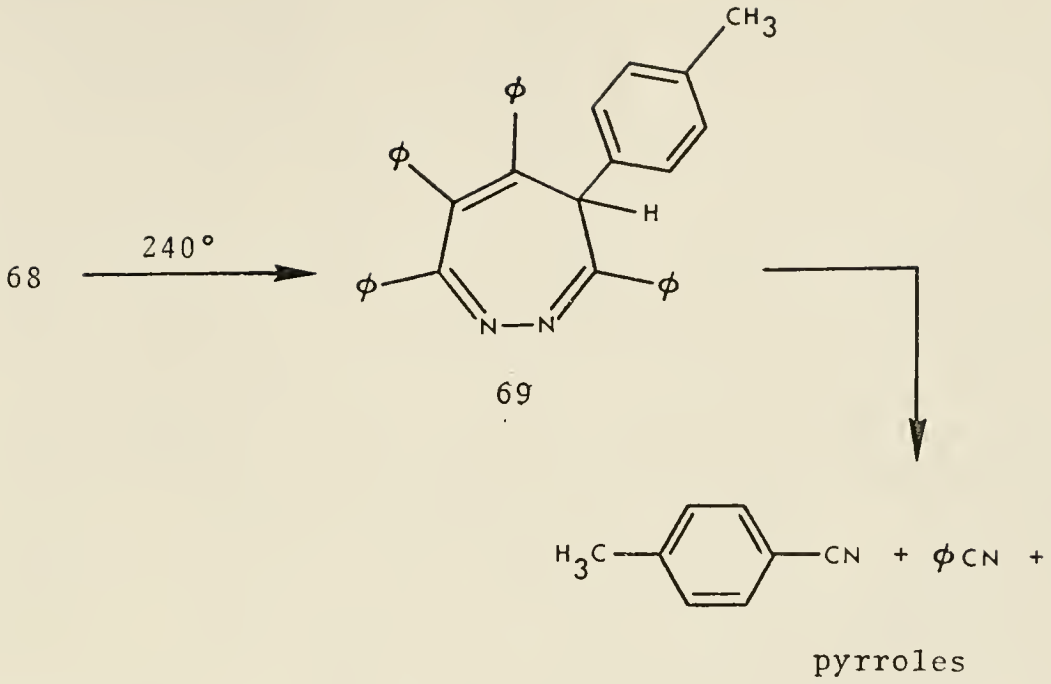

BR2
CA4
CA5
CA3
CA6
CA1
CA2
C1
N2
C2
C3
CC6
CC5
CC4
CC3
CC2
CC1
CB1
CB2
CB2
CB6
CB4
CB5
Me
N1
C5
C4
CD1
CD6
CD5
CD2
CD5
CD4
CE1
CE2
CE6
CE4
CE3
CE5
BR1

In connection with the further reaction of the diazepine systems to produce pyrroles and benzonitriles, some groundwork on the mechanism of this fragmentation was carried out.

As was mentioned at the beginning of the chapter, diazepines which result from the high temperature reaction of sym-triphenylcyclopropene and tetrazines substituted with groups other than unsubstituted phenyl decompose at high temperatures into mixtures of pyrroles and benzonitriles as shown in Scheme 2. Thus, in an as yet unspecified manner (see Chapter II), not only the groups originally on the tetrazine ring but also the 1- and 2-positions of the cyclopropene become involved in the diazepine decomposition.

It was also of interest to ascertain whether or not the 4-phenyl of the diazepine also becomes involved in the decomposition. Toward this end 1,2,5,6-tetraphenyl-7-(4-methylphenyl)-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (68) was prepared. Diazanorcaradiene 68 showed the expected properties which, as demonstrated in the Experimental Section, are quite similar to those for 66.

When 68 was decomposed in the injector port of an analytical gas chromatograph with the column at such a temperature that benzonitrile and p-tolunitrile are separable, p-tolunitrile was detected and identified solely on the basis of its relative retention time. The results are summarized in Scheme 17. It should be stressed that these results on the decomposition of 68, while exciting, are still only tentative.



Scheme 17

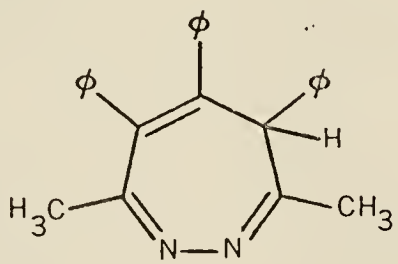
CHAPTER II

MASS SPECTRAL CORRELATIONS

Introduction

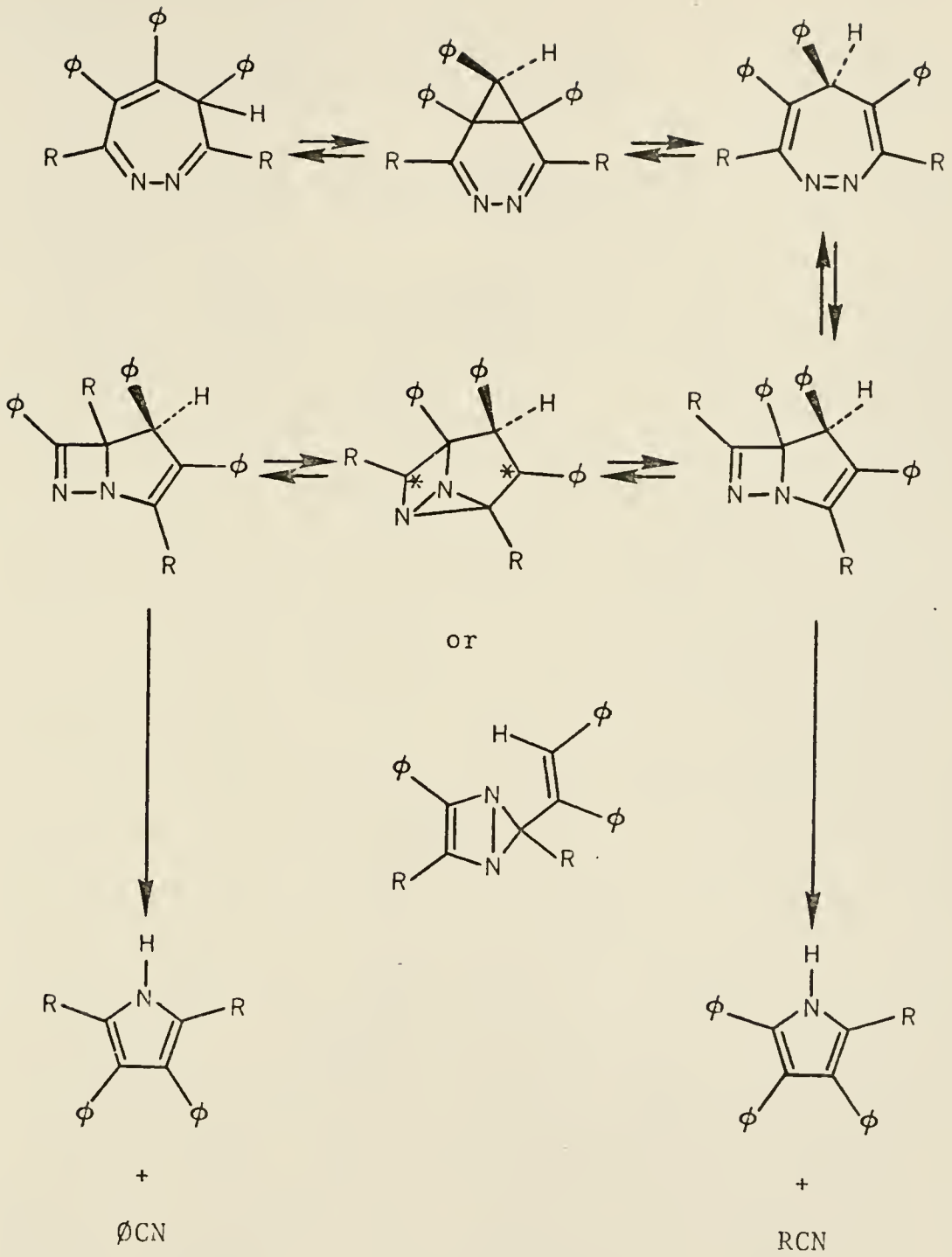
The frequent observation that mass spectral and thermal behavior closely parallel each other for certain compounds is one of the more intriguing aspects of mass spectrometry.[36] It will be the main purpose of this chapter to demonstrate briefly that the thermolytic reactions of Scheme 2 in Chapter I are correlated by the mass spectral behavior of the diazanorcaradienes which rearrange to 4H-diazepines and to attempt to enlighten the mechanism of the 4H-diazepine decomposition.

As shown in Scheme 2, the thermolysis of diazepines such as 70 yields two pyrroles, benzonitrile, and acetonitrile. In the absence of further data, such conversions



70

may be rationalized generally as in Scheme 18.



R = CO_2CH_3

= CH_3

= p-H_3C-C_6H_4

Scheme 18

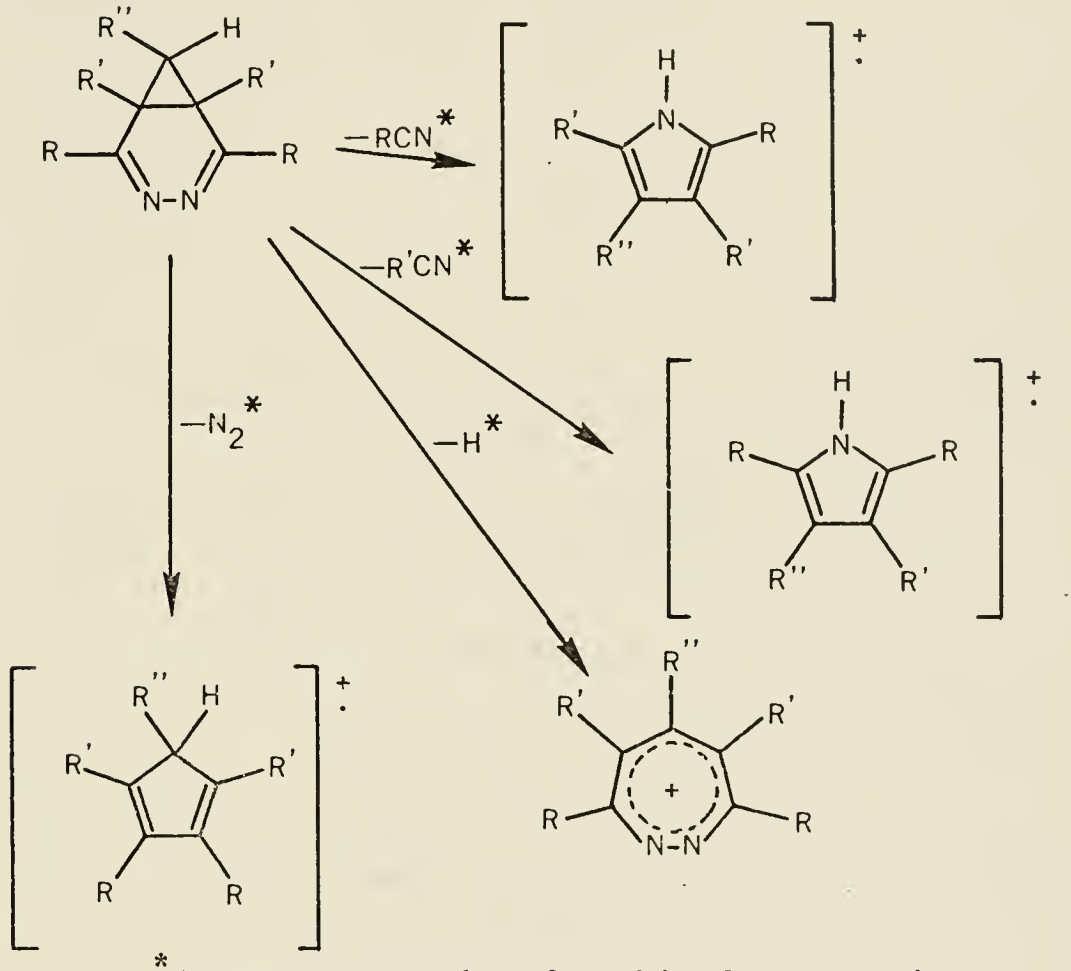
Results and Discussion

The most obvious mass spectral feature of the diazanorcaradienes which undergo thermal rearrangement is their marked similarity to the mass spectra of their respective 4H-diazepines. As examples, the mass spectra of diazanorcaradienes 2 and 66 are plotted in Figures 4 and 6. The mass spectra of the corresponding 4H-diazepines 3 and 67 are given in Figures 5 and 7 respectively. Except for the intensities of some peaks, the mass spectra of 2 and 3 and of 66 and 67 are almost superimposable.

From the above one can arrive at one of three conclusions - the parent ion of the diazanorcaradiene rapidly rearranges to the parent ion of the respective 4H-diazepine, the parent ion of the 4H-diazepine isomerizes to the parent ion of its precursor diazanorcaradiene, or both the diazanorcaradiene and 4H-diazepine parent ions convert into a common intermediate which gives rise to the observed fragmentation pattern.

The mass spectra of all diazanorcaradienes examined, whether they have been observed to rearrange or not, show several similar fragmentations as illustrated in Scheme 19. Table IV gives the intensities for the observed fragmentations of the diazanorcaradienes studied. In those diazanorcaradienes not bearing carbomethoxy or methyl groups in the 2- and 4-positions, loss of benzonitrile or substituted benzonitrile is base peak. All diazanorcaradienes, regardless of substitution or ability to rearrange, show a fairly

intense (2 to 99% of base peak) peak for parent ion ($M^{+\cdot}$) minus nitrogen. Corresponding to this loss of nitrogen



*denotes metastable for this fragmentation

Scheme 19

peak is a flat-top metastable peak which indicates that the nitrogen is lost from the parent ion with the release of a small amount of kinetic energy.[37]

From the above observation that the mass spectra of 4H-diazepines resemble the general diazanorcaradiene mass spectrum, it is tempting to assume that in the mass spectrometer 4H-diazepines derived from diazanorcaradienes revert to their precusor diazanorcaradienes or an ion common to

Table IV

Relative Intensities for Important Mass Spectral Fragmentations of Diazanorcaradienes[a]

	Diazanorcaradiene	-H	$-N_2$	-R'CN	-RCN
2	R=Ø, R'=Ø, R''=Ø[b]	16%[c]	99%[d]	100%	----[e]
71	R=p-I-C_6H_4, R'=Ø, R''=Ø[b]	7%	41%	42%[f]	100%
72	R=CH_3, R'=Ø, R''=Ø[b,g]	28%[h]	39%	4%	100%
10	R=CO_2CH_3, R'=Ø, R''=Ø[b]	11%	51%	33%	66%[h,i]
22	R=CO_2CH_3, R'=Ø, R''=H[j]	16%	2%	5%	20%[k]
21	R=Ø, R'=Ø, R''=H[j]	8%	37%	100%	----[e]
7	R=Ø, R'=H, R''=Ø[j,l]	9%	20%	100%	4%
68	R=Ø, R'=Ø, R''=p-H_3C-C_6H_4[g]	5%	33%	100%	----[e]

[a]The corresponding 4H-diazepine will be the same to ±3% unless otherwise noted. [b]See Table V below for thermal data on this compound or a related compound. [c]Diazepine is 11%. [d]Diazepine is 66%. [e]Same as loss of R'CN. [f]Diazepine is 29%. [g]Corresponding 4H-diazepine not available. [h]See text for a discussion of this intensity. [i]Base peak m/e 291. [j]Does not rearrange to a 4H-diazepine. [k]Base peak m/e 346 (parent ion). [l]In the isomeric diazepine 26[17] the listed fragmentations are respectively 13%, 5%, ----, and 100%.

both. This would lend some credence to the first step of Scheme 18. However, the mass spectra of diazepine 26 and diazanorcaradiene 7 are also quite similar even though, as demonstrated in Chapter I, thermally 7 does not isomerize to 26. It has also been shown that apparently 26 does not decompose into pyrroles and benzonitrile on thermolysis.[38] Thus, in the absence of further information, all that can be said about the diaza species which give rise to pyrroles on thermal decomposition of 4H-diazepines derived from diazanorcaradienes is that the mechanism of Scheme 18 or something similar is not precluded by mass spectral observations.

Although the mass spectra of rearrangeable diazanorcaradienes and, of course, the corresponding 4H-diazepines give no real information on the mechanism of diazepine decomposition to pyrroles, for the most part the mass spectra do follow the thermal decomposition process quite closely. The thermal decomposition data for the four diazepines that have been studied[6] are tabulated in Table V. The mass spectra of the four diazepines or closely related compounds are given in Table IV.

All diazepines formed from the rearrangement of diazanorcaradienes show intense mass spectral peaks for pyrroles formed by electron-impact-induced decomposition of $M^{+}\cdot$. At least as far as low-resolution mass is concerned, the pyrroles formed in the mass spectrometer correspond to those formed by the thermal process of Scheme 18. The base peak

in the mass spectrometer is always $M^{+\cdot}$ minus benzonitrile or substituted benzonitrile except when the azine linkage is substituted with carbomethoxy or methyl groups. It will be noted that thermally 3,7-bis(p-tolyl)-4,5,6-triphenyl-4H-1,2-diazepine (73), which is related to 71 decomposes into an approximately equimolar mixture of pyrroles resulting from loss of benzonitrile and p-tolunitrile. In the mass spectrometer diazepine 71 loses approximately three times as much p-iodobenzonitrile as benzonitrile. The above facts may be rationalized by considering that thermally 73 (or 71) can lose nitriles RCN and R'CN only from bicyclic forms similar to 8 (see Preface and Scheme 18), whereas in the mass spectrometer the diazepine can lose RCN from the open form or the bicyclic form but can lose R'CN only by isomerizing through the bicyclic form. It will be again noted that the diazepine 26 does not result from the thermal isomerization of a diazanorcaradiene nor has it been possible to thermally decompose it into benzonitrile and pyrrole, but yet, in the mass spectrometer, loss of benzonitrile is base peak.

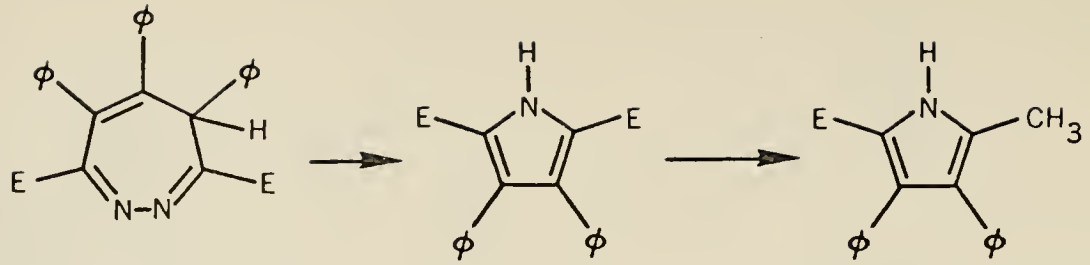
Table V

Thermal Decomposition Data for Some 4H-Diazepines[6]

Diazepine	-ØCN	-RCN[a]
3[b]	100%	----
11	>98%	----[c]
73	49%	51%[d]
70	67%	33%

[a]R is the group originally on the 3- and 7-positions of the diazepine. The other three positions of the diazepine are substituted with phenyls. [b]Can only lose benzonitrile. [c]None detected. [d]A small amount of unidentified liquid (not benzonitrile or p-tolunitrile) was detected in this decomposition.

The mass spectra of diazepine 11 and its related diazanorcaradiene 10 (Figure 8) show 71% and 65% peaks for, respectively, loss of methyl cyanoformate and loss of benzonitrile from the parent ion. The base peak corresponds to what may be formally described as the decarboxylation product of the pyrrole formed by loss of benzonitrile from the parent ion as depicted in Scheme 20. Thermally, diazepine 11 converts exclusively into dimethyl 3,4-diphenylpyrrole-2,5-dicarboxylate, which is the end result of loss of benzonitrile from 11.[6] Again the loss of methyl cyanoformate from the parent ion of 11 may be due to fragmentation from the open diazepine form as opposed to



Scheme 20

fragmentation from a bicyclic form and thus have no thermal analogy.

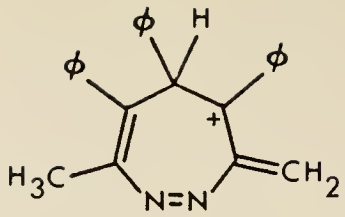
In the mass spectrum of the diazanorcaradiene related to 70 (72), loss of acetonitrile from the parent ion is base peak but loss of benzonitrile from the parent ion gives only a 3% peak! Thermally the diazanorcaradiene 72 converts into 70 only with difficulty relative to cases where the diazanorcaradiene azine linkage is substituted with phenyls or carbomethoxy groups. Also with difficulty, 70 thermally converts into a 2.17:1 molar mixture of, respectively, 2,5-dimethyl-3,4-diphenylpyrrole and 1-methyl-2,3,4-triphenylpyrrole.[6] Thus, thermally, loss of benzonitrile is the predominant pathway. The combination of the loss of acetonitrile from the unrearranged form of the diazanorcaradiene 72 in the mass spectrometer and the difficulty with which the diazanorcaradiene rearranges to 70 may be used to rationalize the unusually low abundance of the loss of benzonitrile from the parent ion in the mass spectrum

of the diazanorcaradiene 72. At the time of this writing no mass spectrum of 70 was available.

As a further complication to the diazepine decomposition problem, it was shown tentatively in Chapter I that, on thermolysis, diazanorcaradiene 68 presumably reacting *via* diazepine 69 yields tolunitrile in addition to the expected benzonitrile.

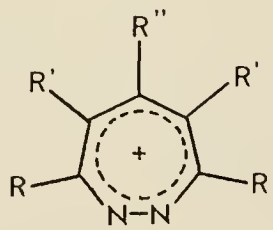
The mass spectrum of 68 shows a peak for the loss of tolunitrile from the parent ion as depicted in Figure 9. The loss of tolunitrile from the parent ion is supported by a metastable peak but, unfortunately, the metastable can also be accounted for by loss of methyl from the parent minus benzonitrile ion. A similar problem arises in the interpretation of the mass spectrum of diazanorcaradiene 66 and its related diazepine 67 (Figures 6 and 7).

In closing this chapter it will be noted that the mass spectra of all diazanorcaradienes and diazepines examined show a P-1 peak of 5-28% intensity (see Table IV). In all cases except when the azine linkage is substituted with methyl groups the P-1 intensity is only 5-16%. It is assumed that the hydrogen lost is the one at C-7 in diazanorcaradienes and C-4 in diazepines except when the azine linkage is substituted with methyl groups, which opens the possibility of loss of hydrogen from one of the methyl groups to form an ion such as 74.



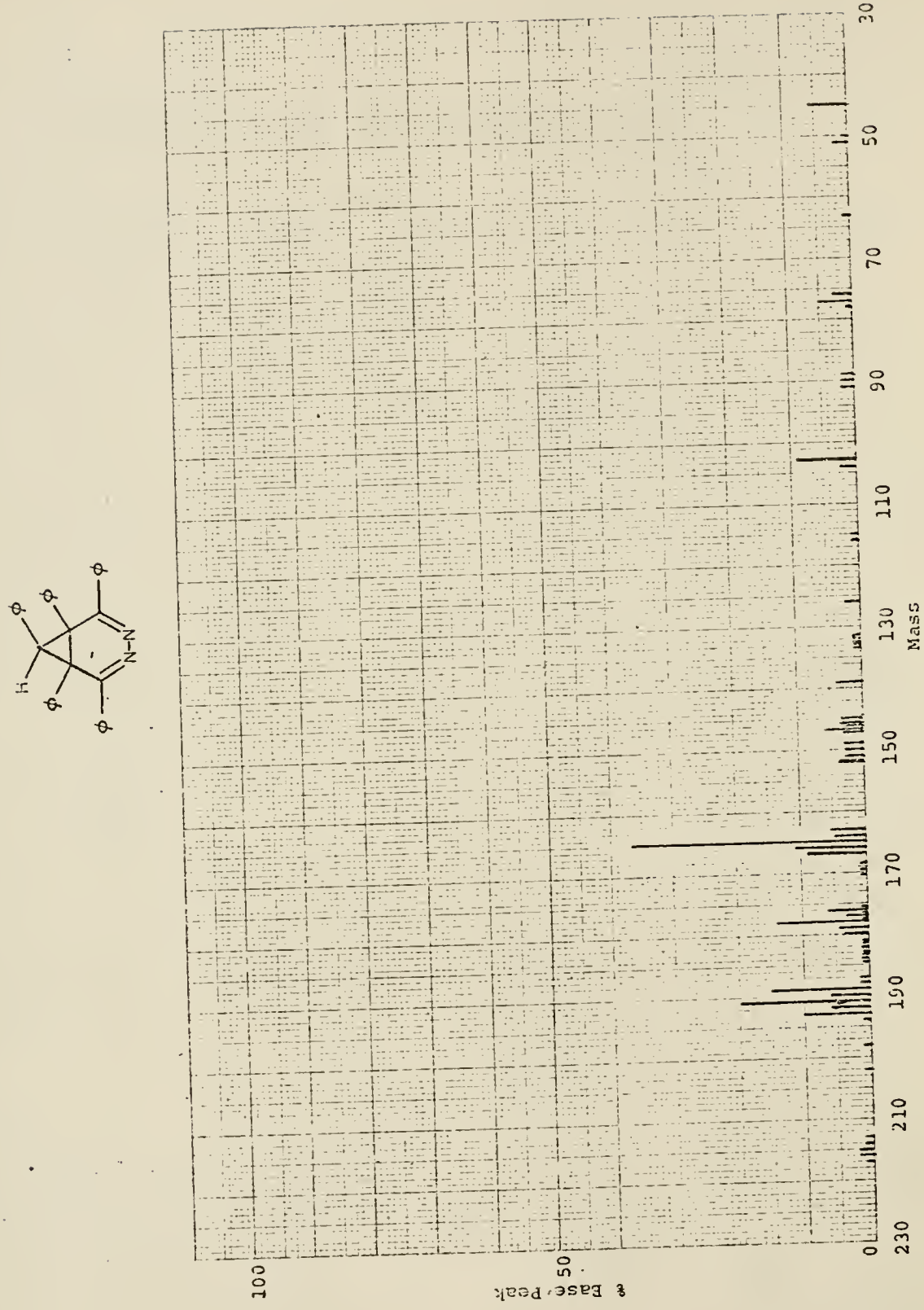
74

Although some of the driving force for loss of a hydrogen radical from the parent ion is conversion from the odd-electron $M^{+\cdot}$ to the even electron P-1 ion, perhaps another driving force may be formation of the aromatic diazatropylium cation 75. It is noteworthy that in the mass spectrum of cycloheptatriene, which is known to easily convert into the aromatic tropylium cation, base peak is loss of hydrogen radical.[39] The diazatropylium problem will be discussed more fully in Chapter IV.



75

Figure 4. Mass spectrum of 1,2,5,6,7-pentaphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (2)


100
50
0
% Base Peak
30
50
70
90
110
130
150
170
190
210
230
Mass

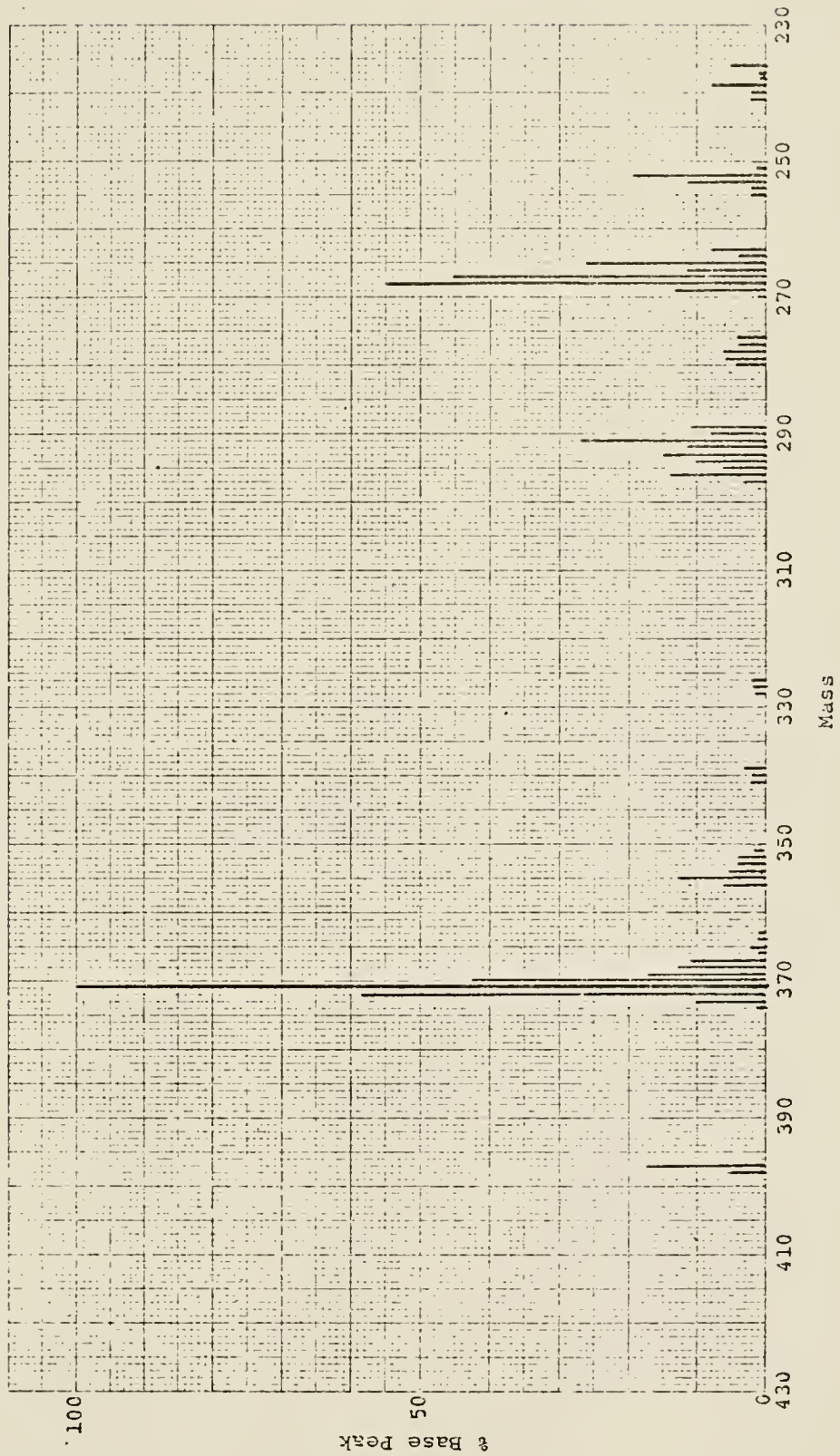


Fig. 4 continued

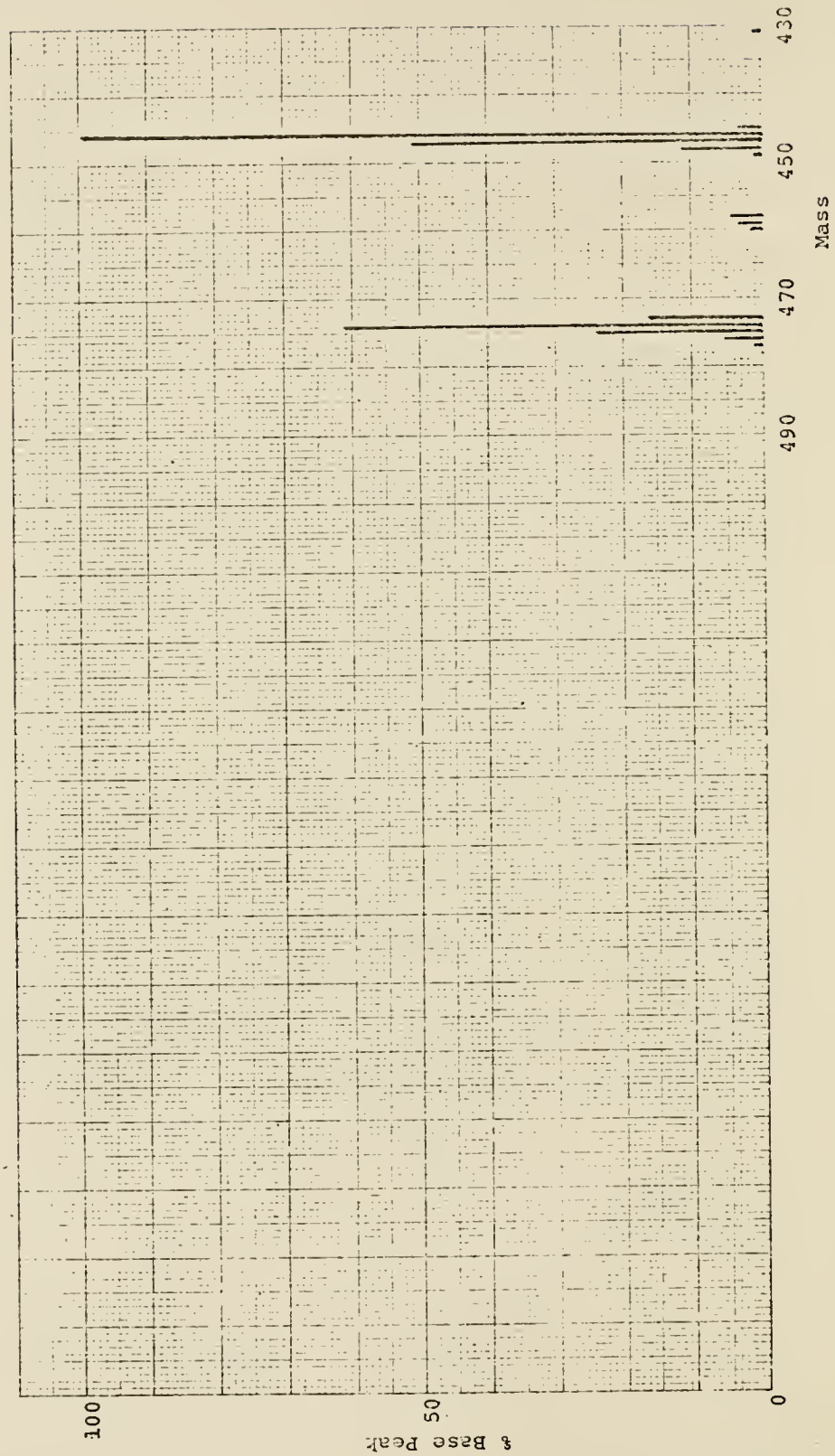
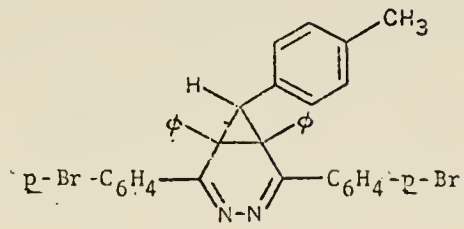
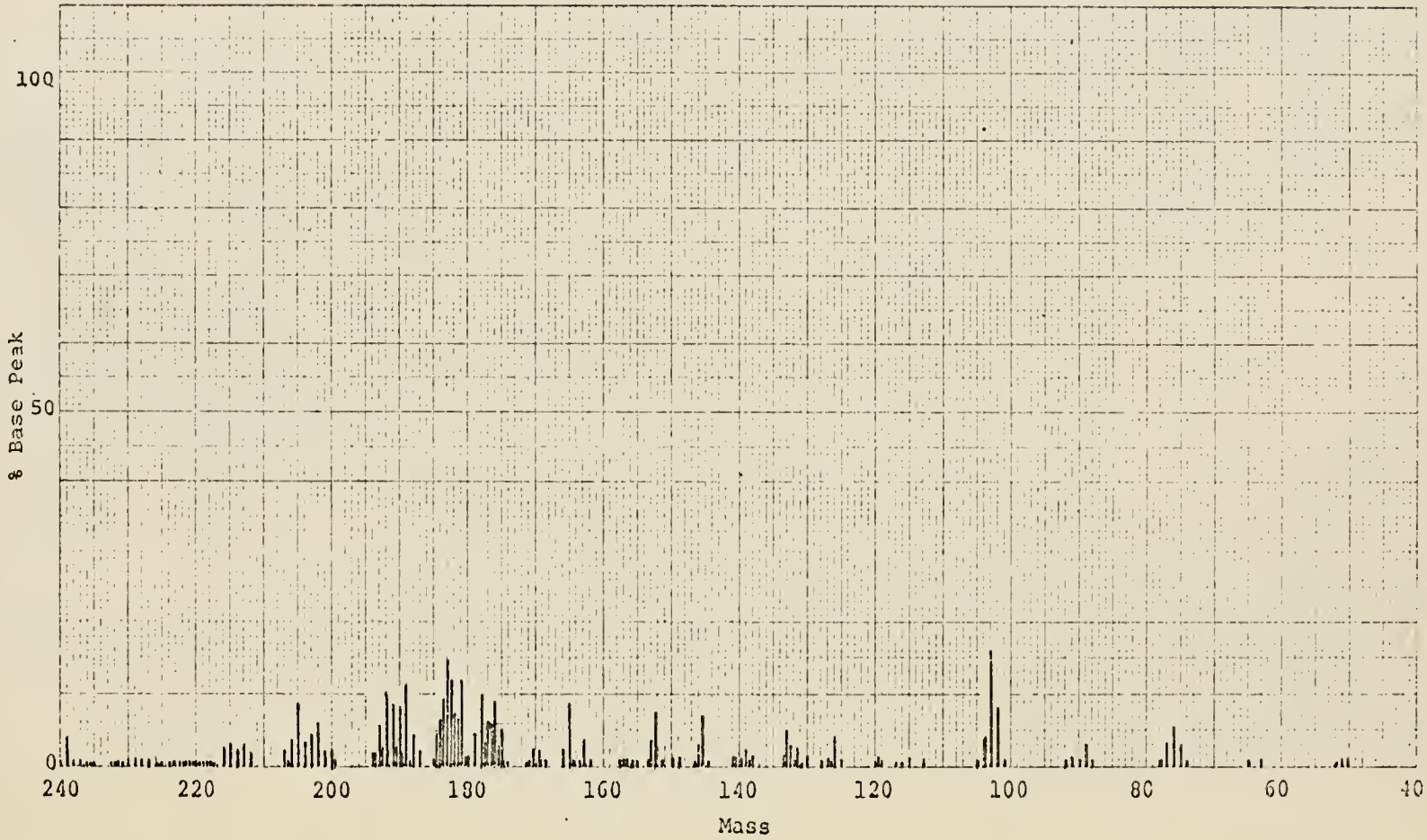


Fig. 4 continued

Figure 5. Mass spectrum of 2,5-bis(4-bromophenyl)-7-(4-methylphenyl)-1,6-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (66)


CH3
H
ϕ
ϕ
p-Br-C6H4
C6H4-p-Br
N-N


100
50
0
% Base Peak
240
220
200
180
160
140
120
100
80
60
40
Mass

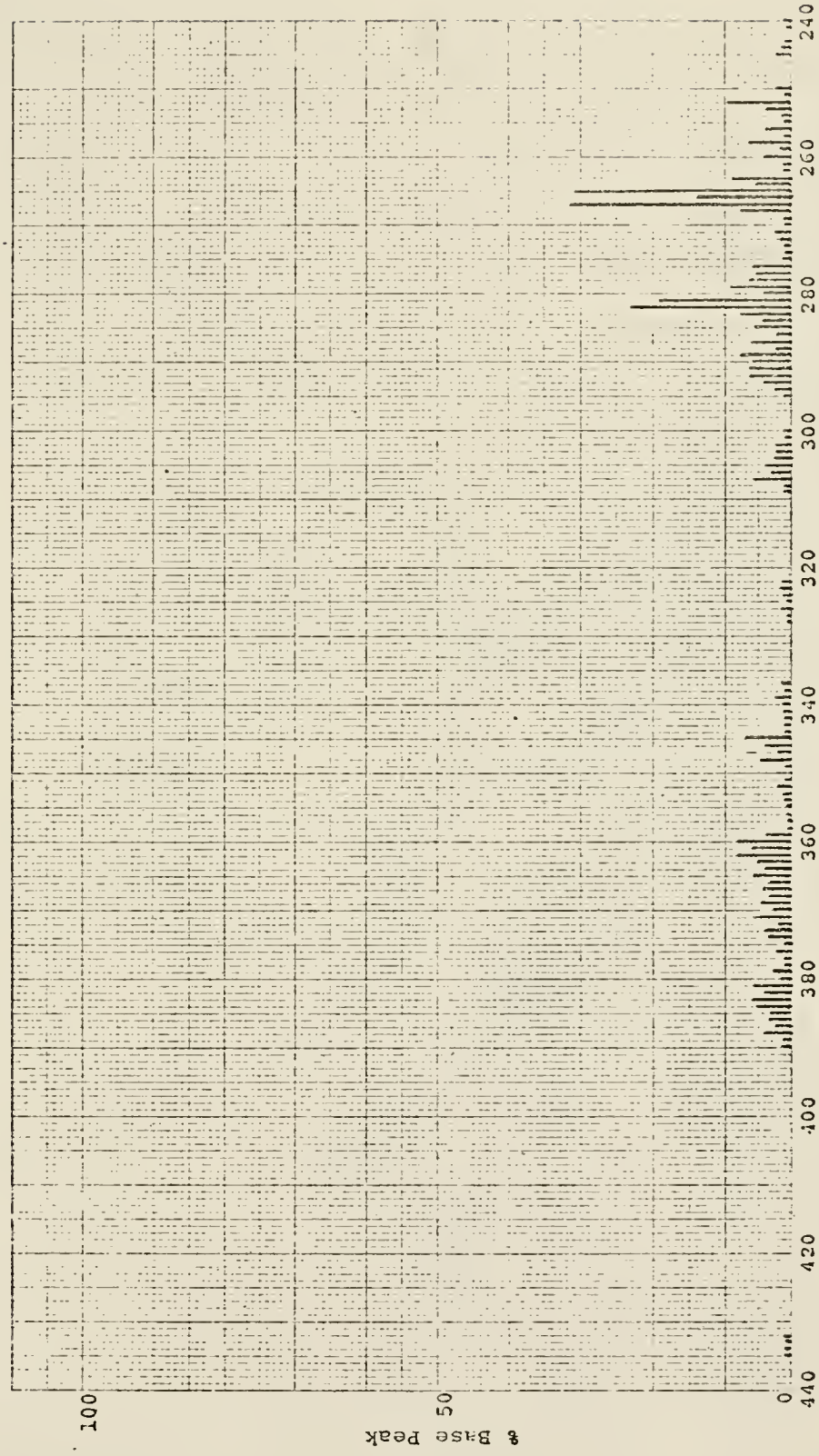


Fig. 5 continued

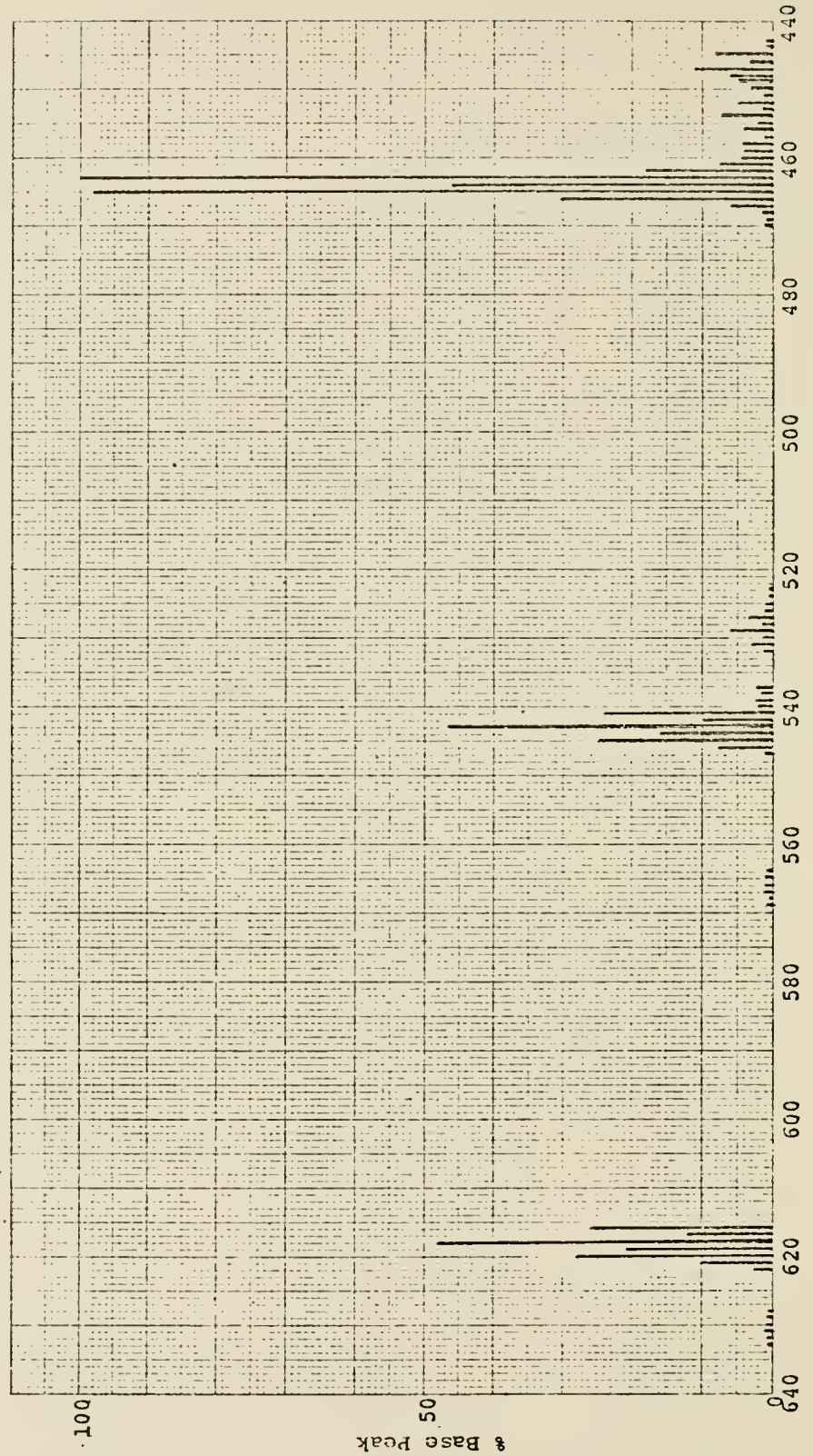


Fig. 5 continued

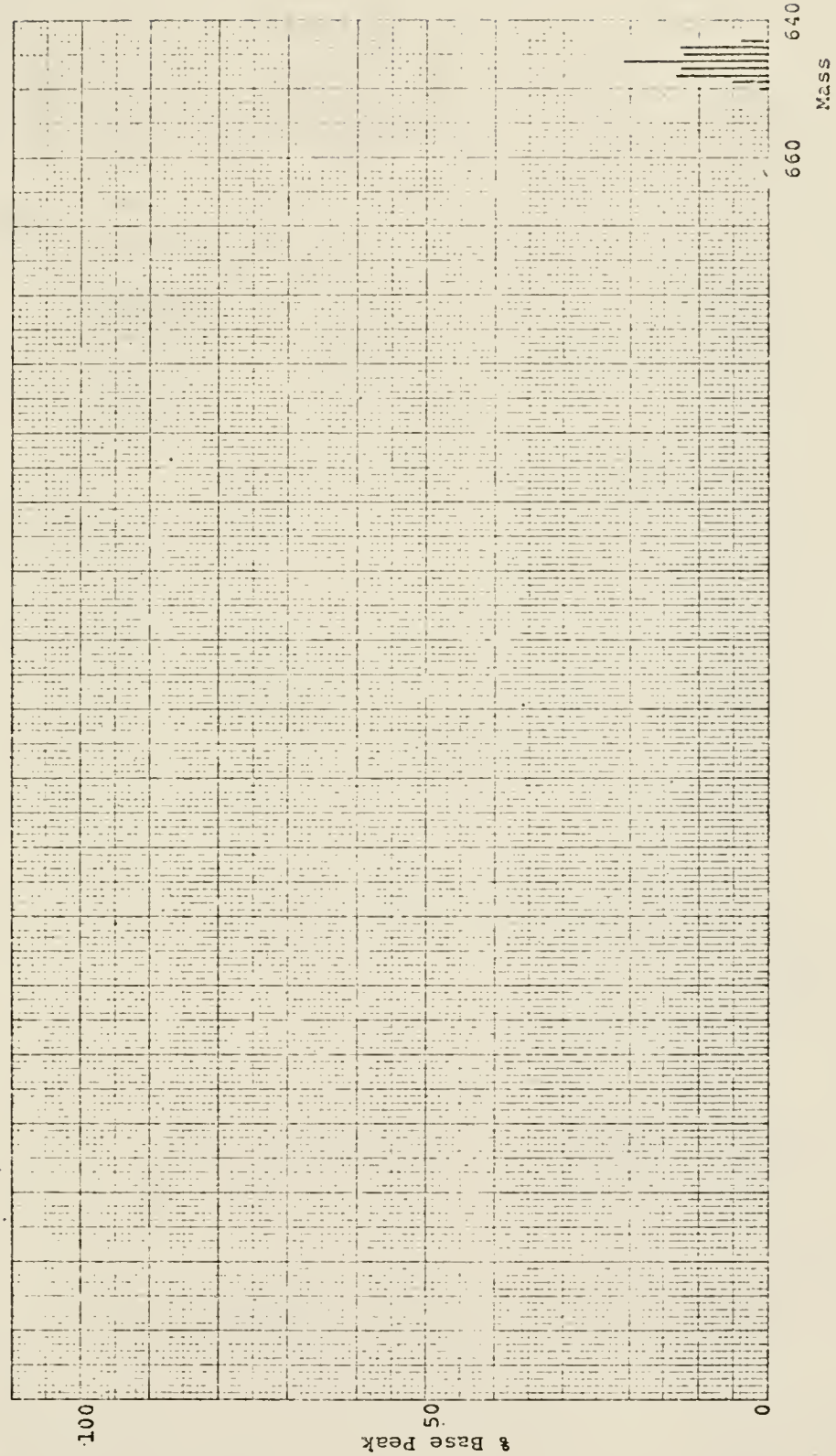
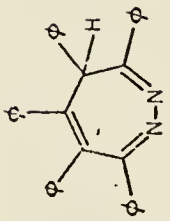
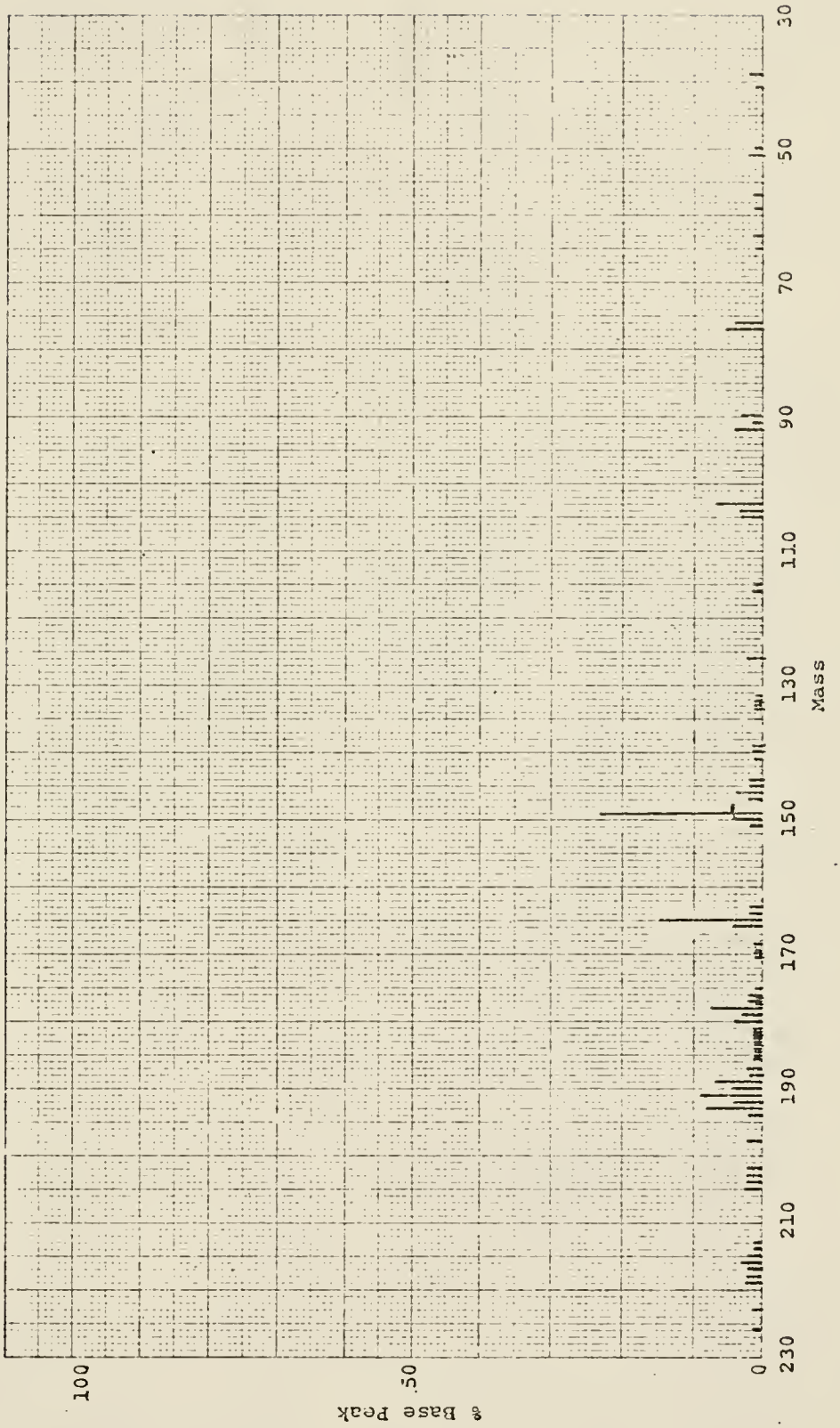


Fig. 5 continued

Figure 6. Mass spectrum of 3,4,5,6,7-pentapheny1-4H-1,2-diazepine (3)


H
N
N


% Base Peak
100
50
0
30
50
70
90
110
130
150
170
190
210
230
Mass

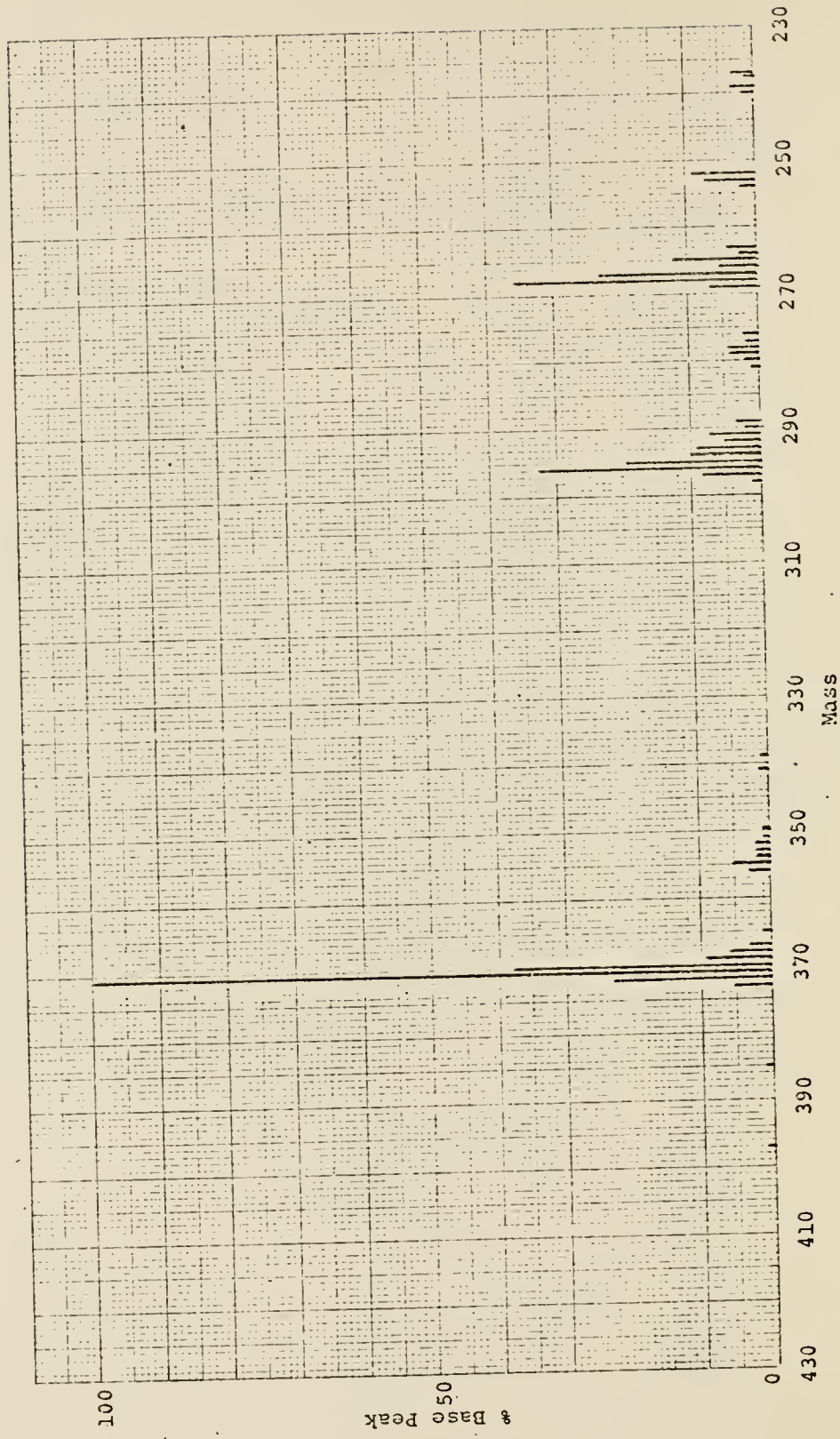


Fig. 6 continued

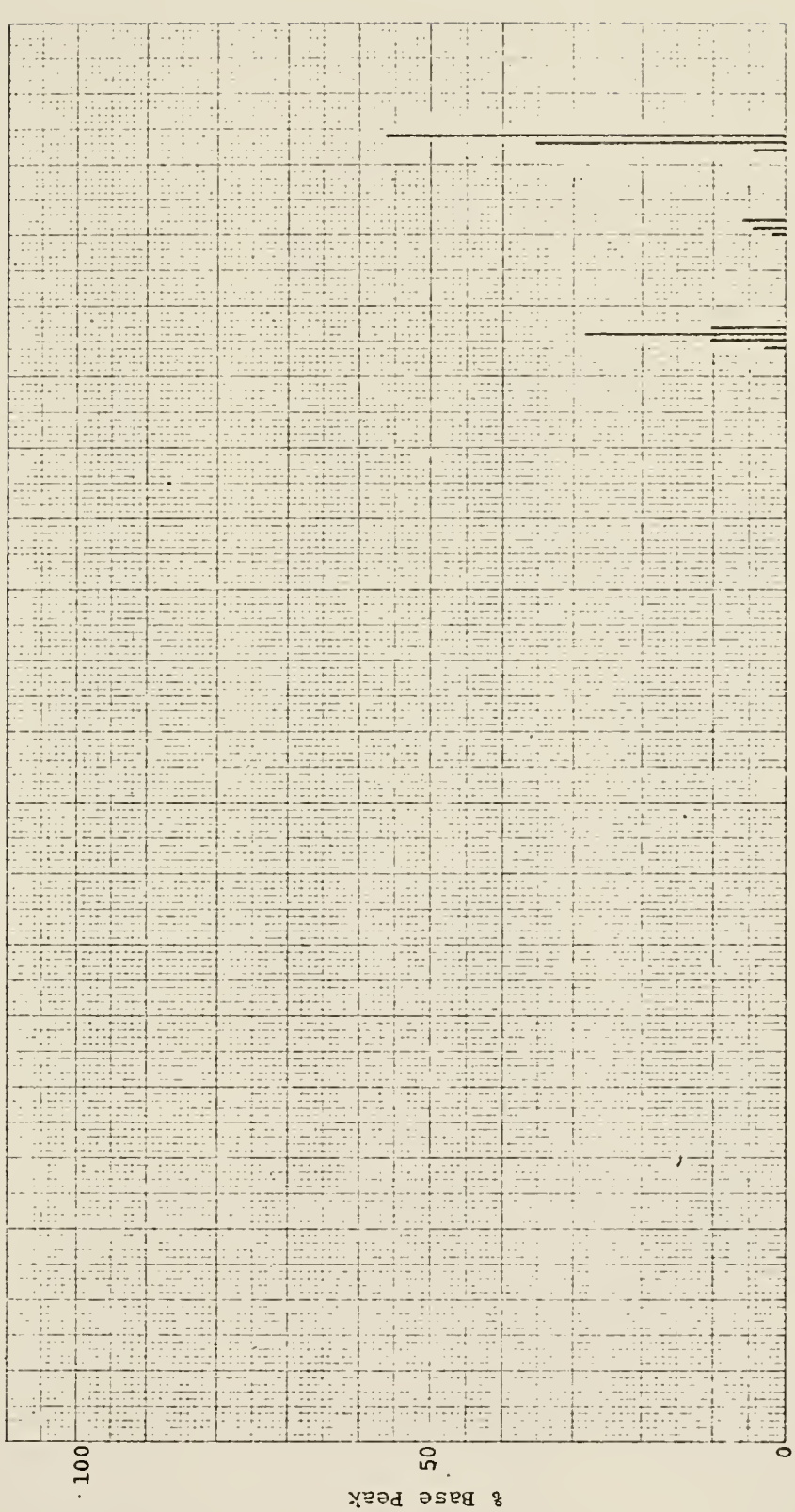
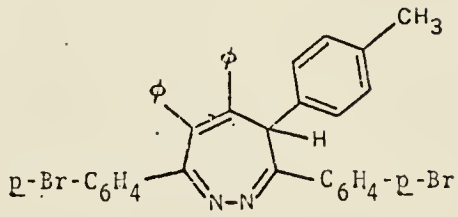
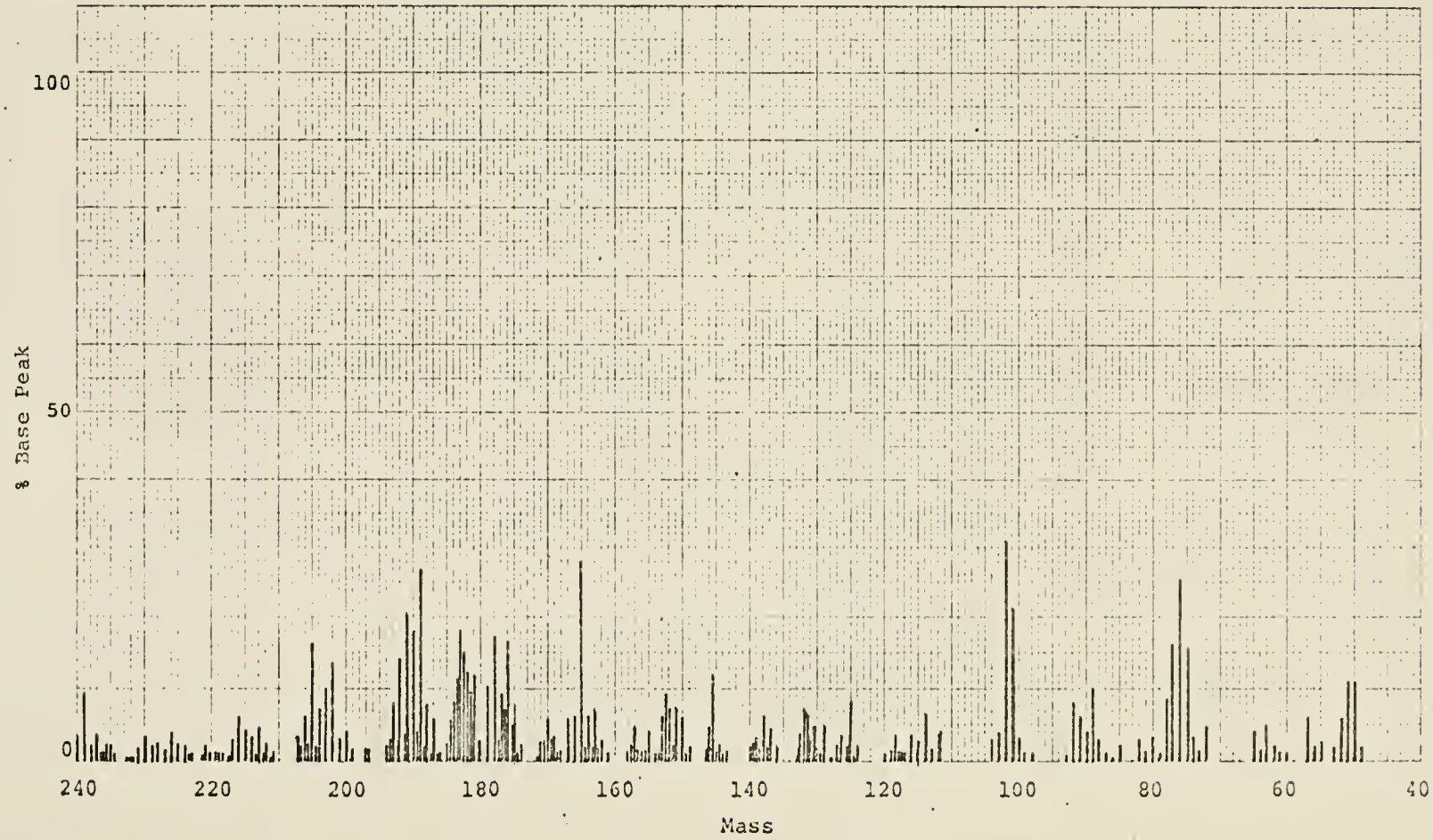


Fig. 6 continued

Figure 7. Mass spectrum of 3,7-bis(4-bromophenyl)-4-(4-methylphenyl)-5,6-diphenyl-4H-1,2-diazepine (67)


CH3
ϕ
ϕ
H
p-Br-C6H4
N-N
C6H4-p-Br


100
50
0
% Base Peak
240
220
200
180
160
140
120
100
80
60
40
Mass

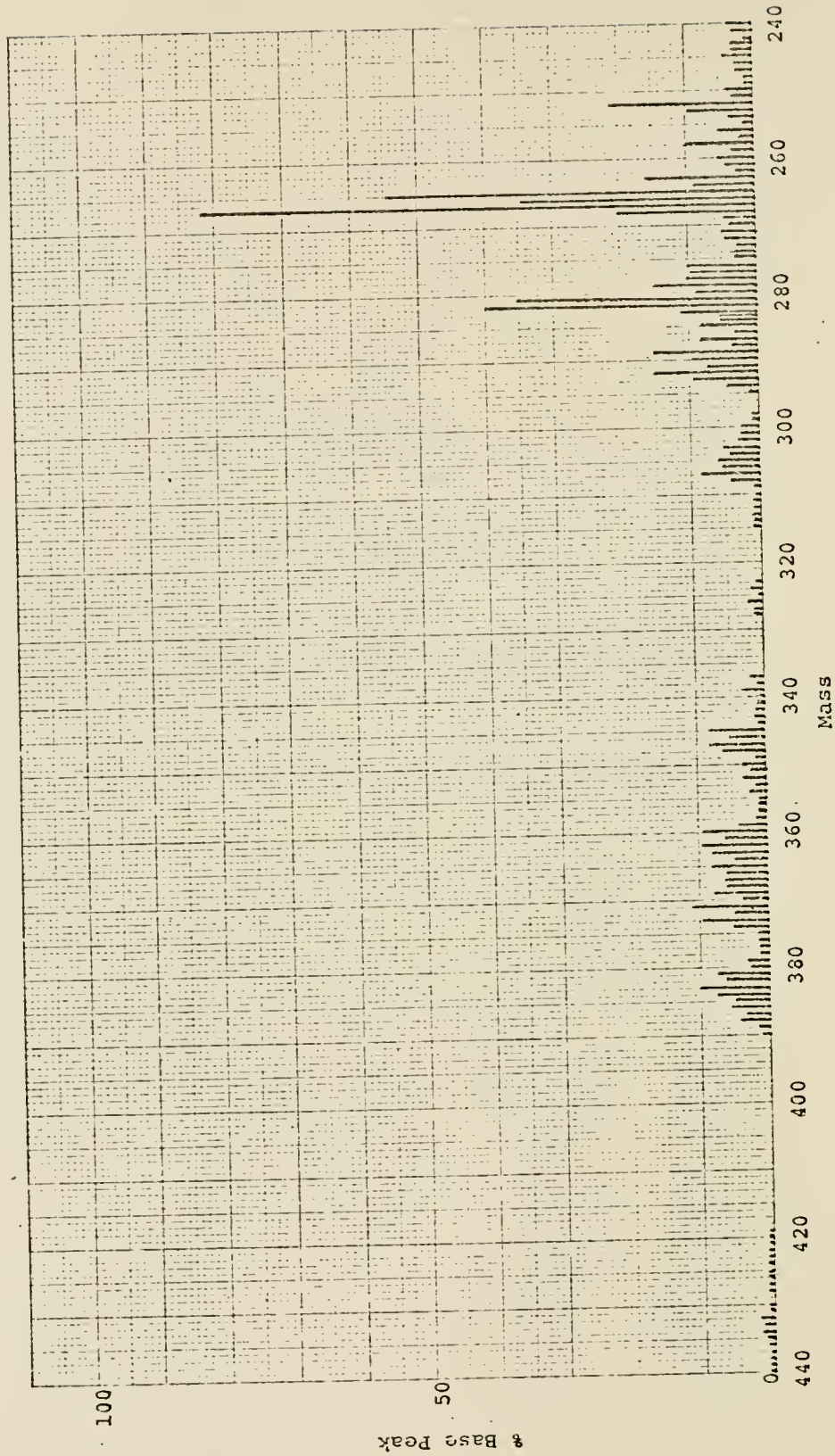


Fig. 7 continued

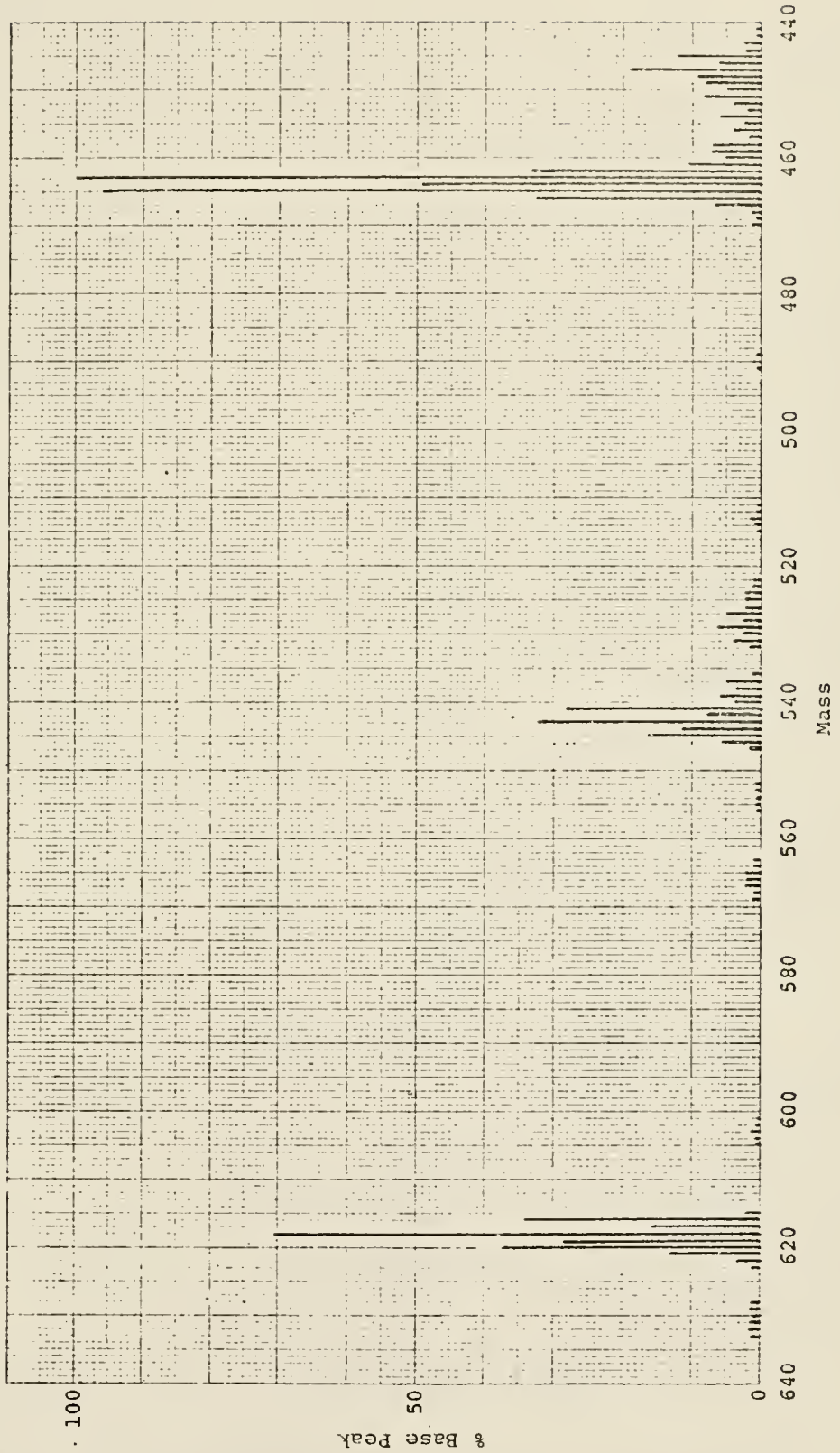


Fig. 7 continued

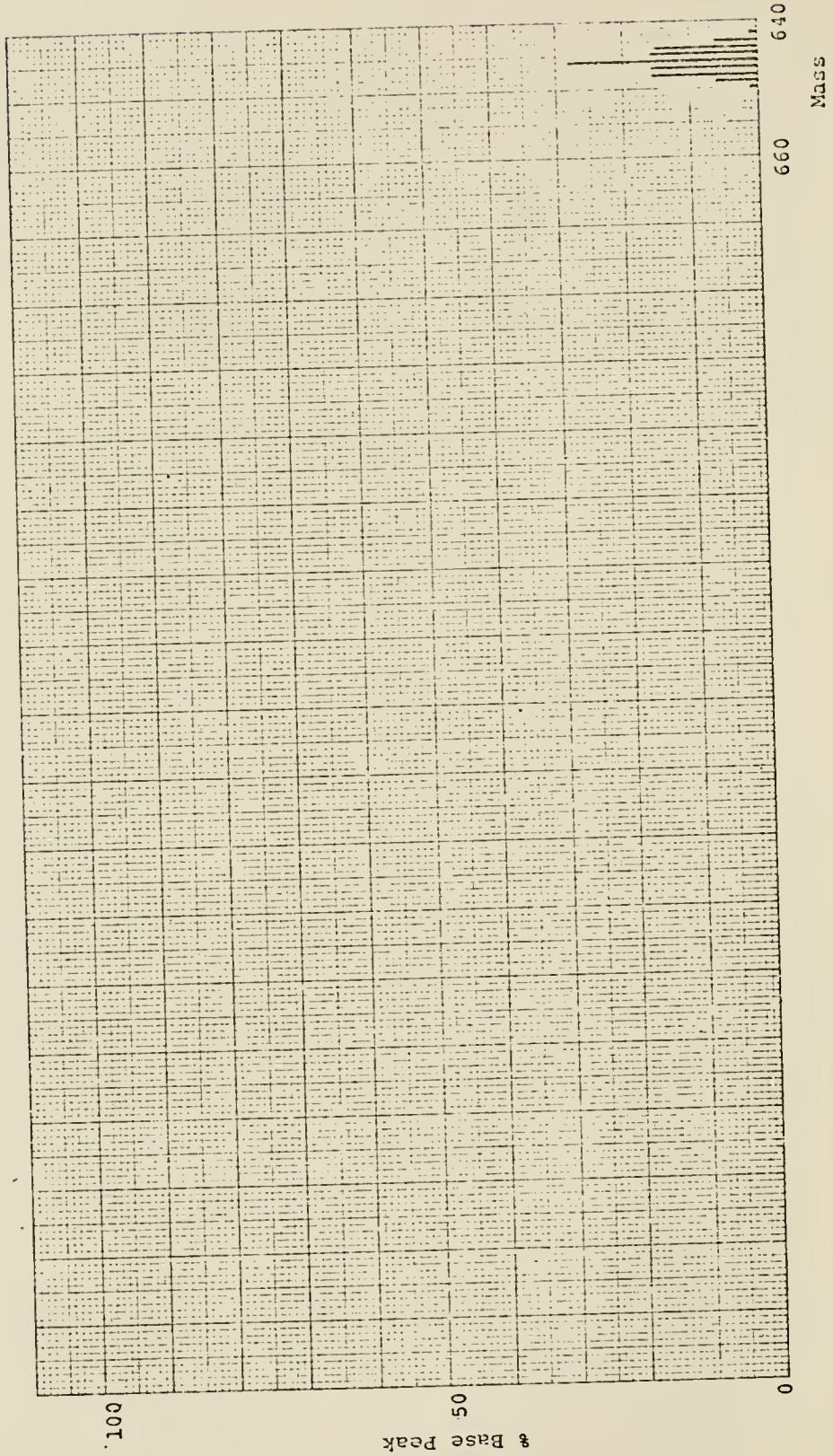
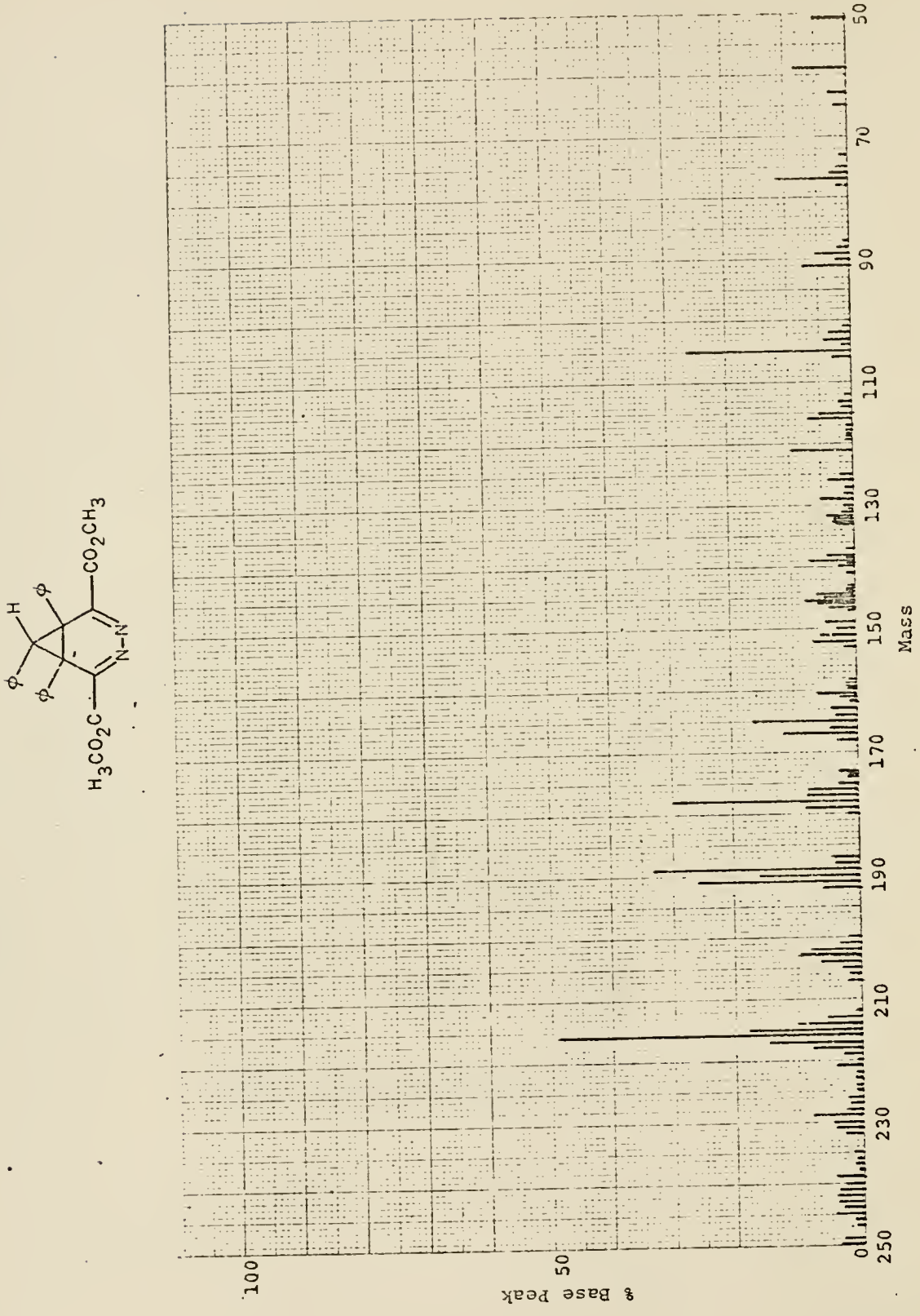


Fig. 7 continued

Figure 8. Mass spectrum of dimethyl 1,6,7-triphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5-dicarboxylate (10)


H
Φ
Φ
Φ
CO2CH3
N-N
H3CO2C
% Base Peak
100
50
0
50
70
90
110
130
150
170
190
210
230
250
Mass

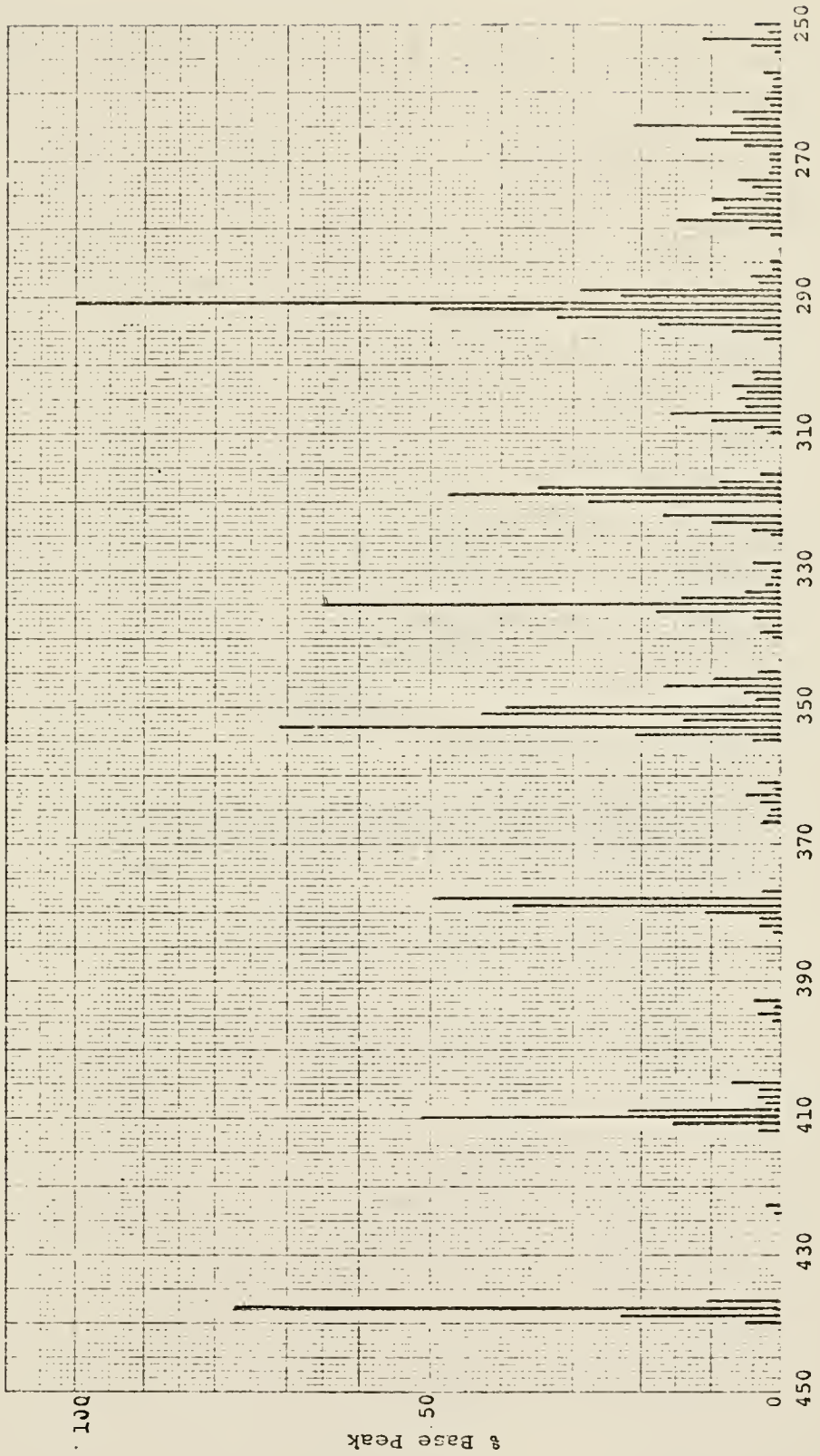
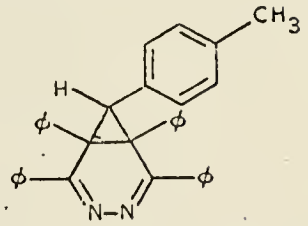
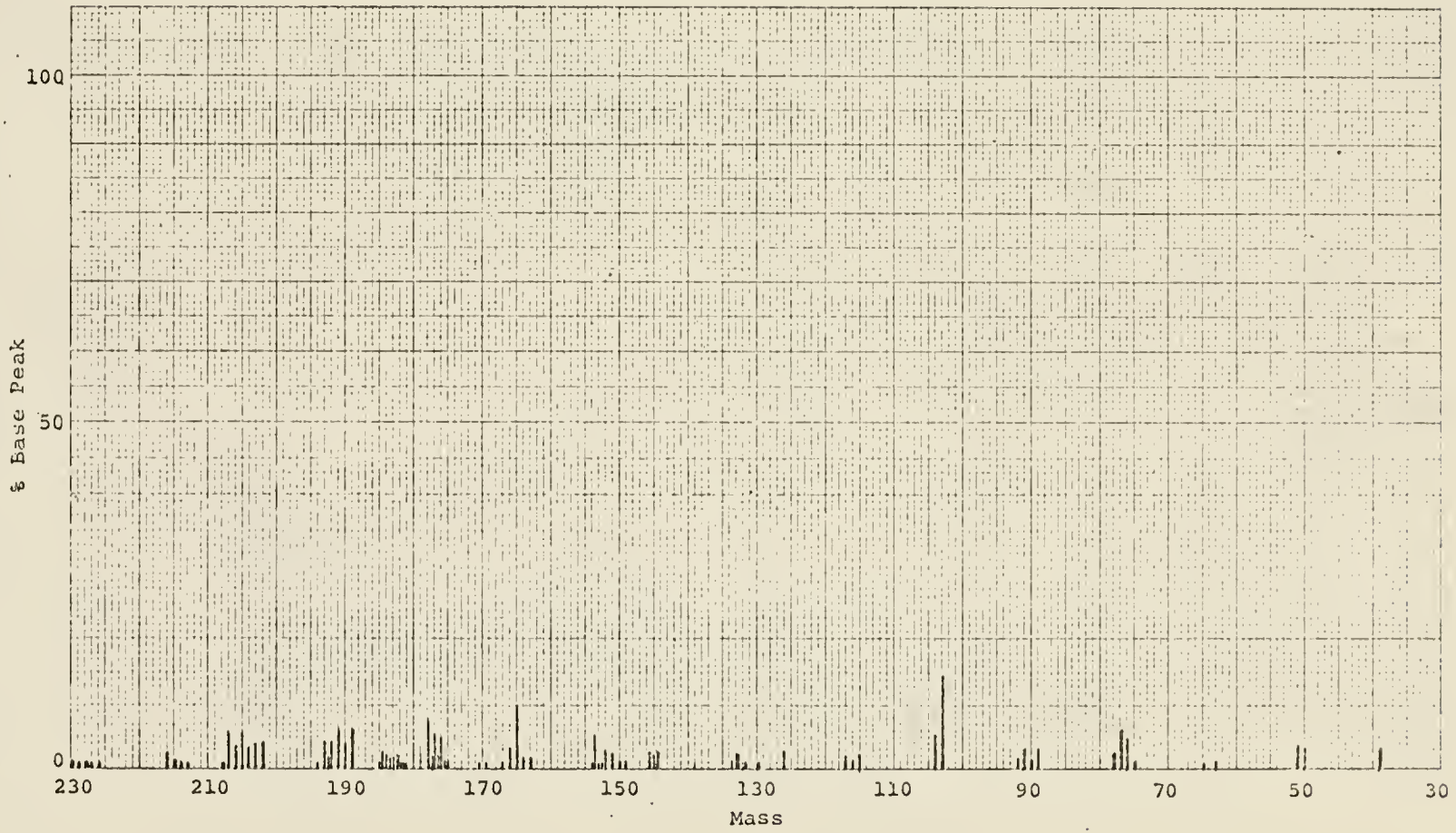


Fig. 8 continued

Figure 9. Mass spectrum of 7-(4-methylphenyl)-1,2,5,6-tetraphenyl-3,4-diazabicyclo-[4.1.0]hepta-2,4-diene (68)


CH3
H
ϕ
ϕ
ϕ
ϕ
N–N


100
50
0
% Base Peak
230
210
190
170
150
130
110
90
70
50
30
Mass

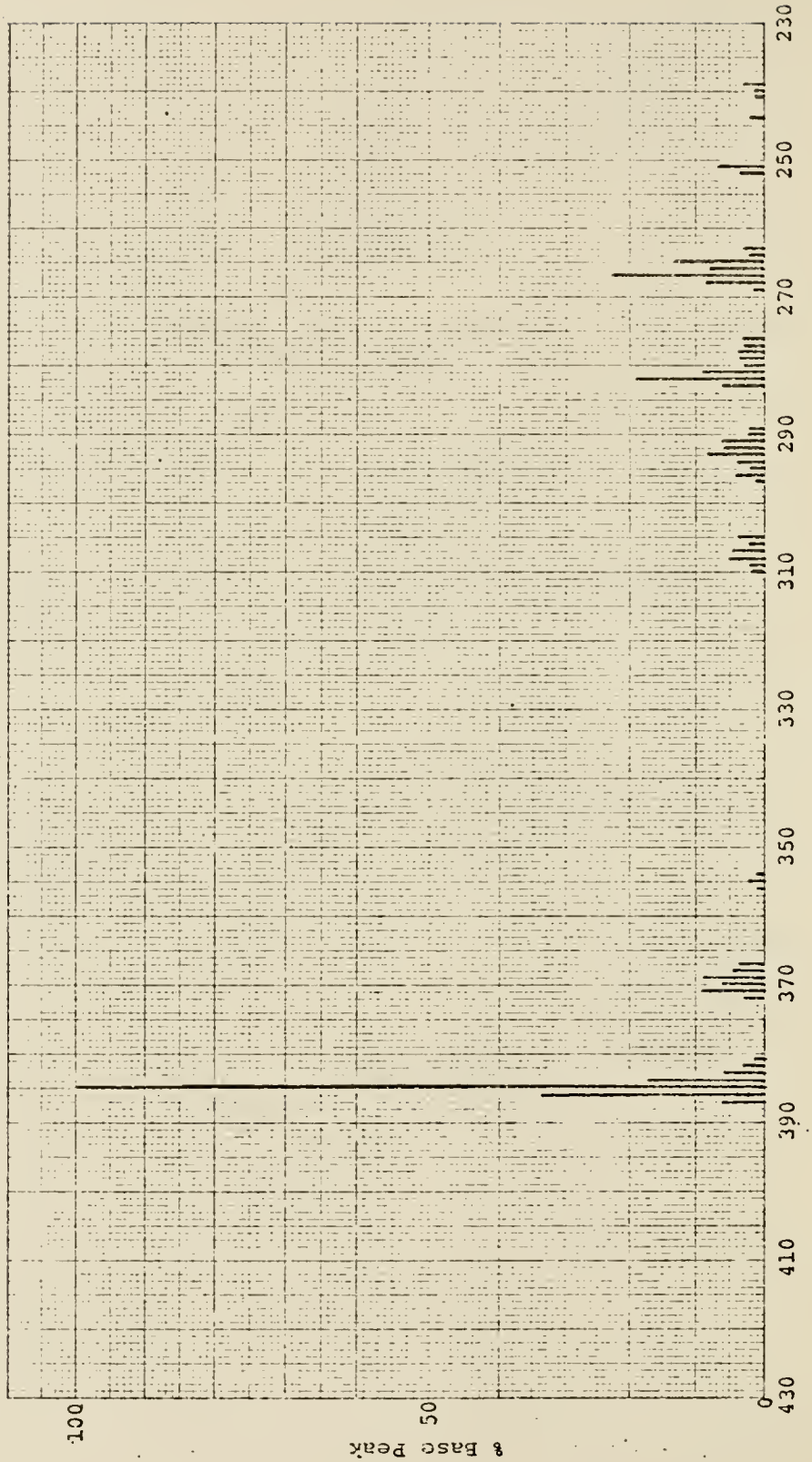


Fig. 9 continued

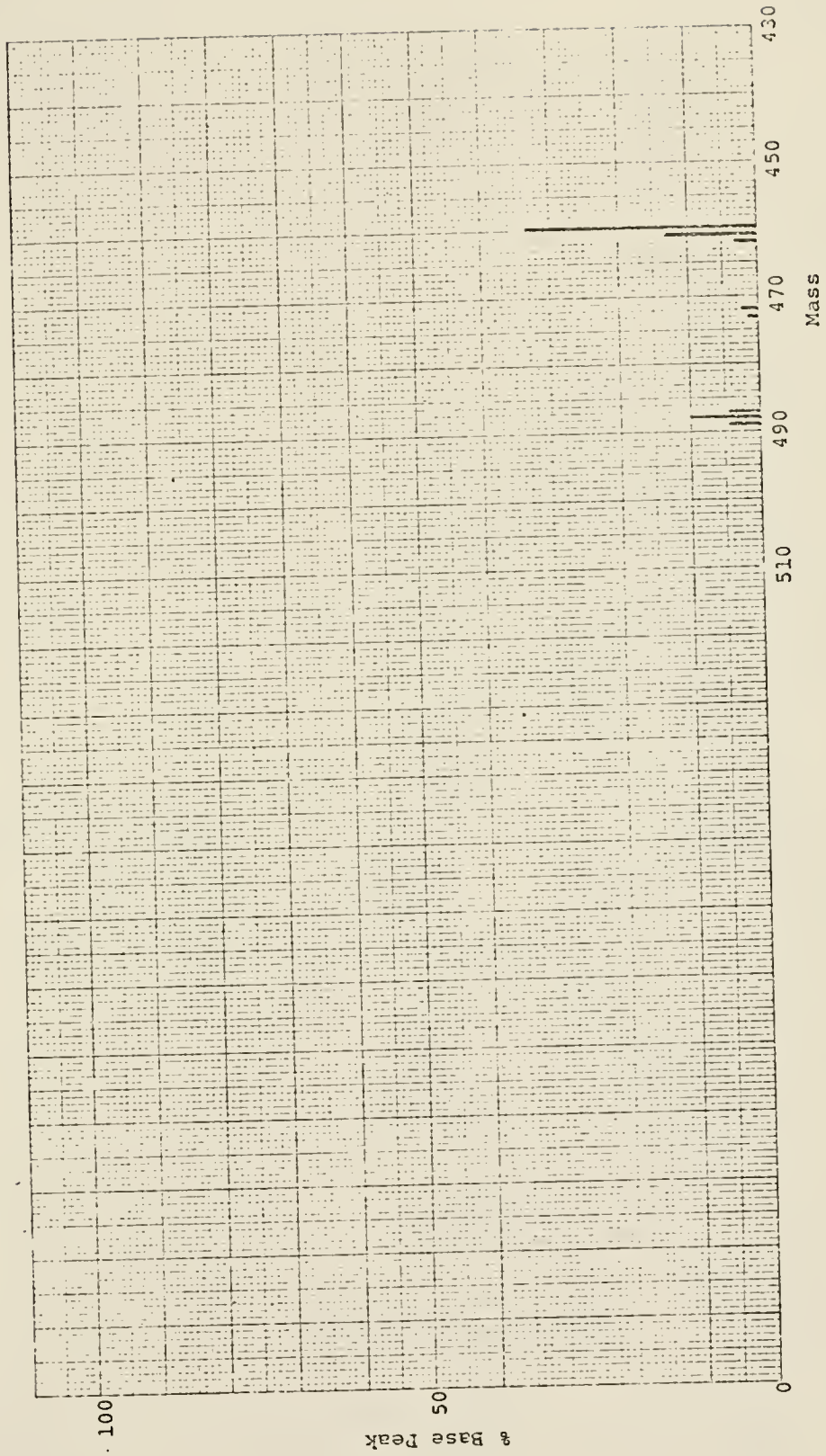


Fig. 9 continued

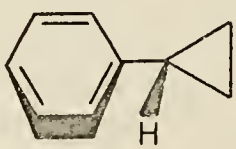
CHAPTER III

CYCLOPROPYL CONJUGATION IN HETEROAROMATIC SYSTEMS

Cyclopropyl Conjugation

The phenomenon of cyclopropyl conjugation is quite well known[40] and has been extensively investigated in both the ground state and excited state of many molecules.

Closs and Klinger[41] observed that with decreasing temperature the ortho protons in cyclopropylbenzenes show increased shielding. The increased shielding was attributed to increased population of the bisected, electronically favorable conformation 76.

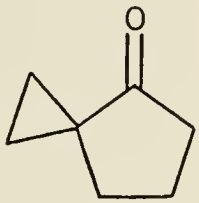


76

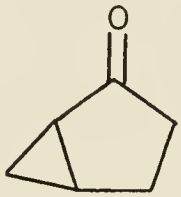
Electron diffraction[42] and infrared spectroscopy[43] also have been employed to detect cyclopropyl conjugation in unsaturated molecules which are in their ground state.

Kosower and Ito[44] found that the excited states of ketones are stabilized by the presence of a cyclopropyl ring alpha to the carbonyl carbon if the geometry is correct. In ketone 77 the geometry is correct for cyclopropyl

conjugation as the cyclopropyl ring is in the bisected configuration. The geometry is far from ideal in ketone 78. Interaction in the excited state was found to lower



77



78

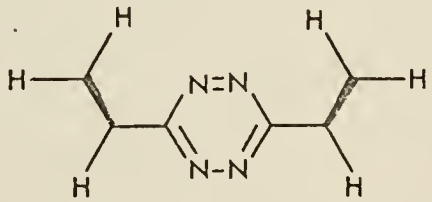
the excited state of 77 by 7-8 kcal/mole relative to the excited state of 78.

As a general rule, it has been found that, in the absence of geometric factors, weak cyclopropyl conjugation is a consequence of poor electron-withdrawing ability of the unsaturated group to which the cyclopropane ring is attached.[45] In other words, the greater the electron demand of the molecule to which the cyclopropane ring is attached, the greater will be the conjugation of the cyclopropane ring with that molecule. Also, it has been shown that the extent of cyclopropyl conjugation is a function of geometry only if the group interacting with the cyclopropane ring is sufficiently electron-withdrawing.[45]

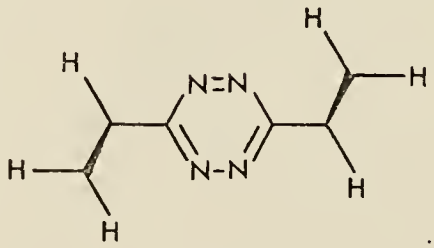
The compounds to be investigated, 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) and 3,6-dicyclopropylpyridazine (80), are both similar to monocyclopropylbenzene studied by Closs and Klinger[41] in that the cyclopropyl rings are

both bonded to an aromatic six-membered ring. There are definite interesting differences though.

Tetrazine 79 contains four nitrogens in the aromatic ring which, accordingly, should enhance cyclopropyl conjugation with the tetrazine ring due to the great electron-withdrawing power of the tetrazine ring. Also, unlike cyclopropylbenzene, the tetrazine ring of 79 carries no hydrogens and, thus, there are negligible steric factors. The only complication is that, assuming the dicyclopropyltetrazine is completely in the bisected form, two conformations are possible which may complicate the NMR spectrum of 79. The top view of the hypothetically possible <u>syn</u> and <u>anti</u> conformations is illustrated below as structures 81 and 82 respectively.



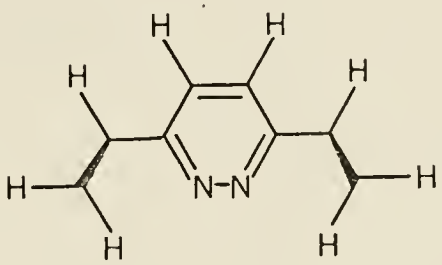
81



82

The pyridazine 80 should exhibit cyclopropyl conjugation similar to that of tetrazine 79 but reduced somewhat due to replacement of two nitrogens by less electron-withdrawing C-H groups <u>i.e.</u> the conjugation in 80 should be intermediate between that of cyclopropylbenzene and tetrazine 79. Also, in the case of 80, steric effects again

are operative as in cyclopropylbenzene since the pyridazine ring has a hydrogen in both the 4- and 5-positions. Assuming the bisected form for 80 the syn rotamer 83 should be favored over the syn rotamer with both cyclopropyl methylene functions interacting with the hydrogens of the pyridazine ring or either of the trans rotamers.



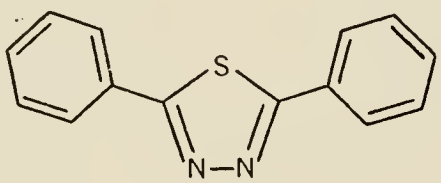
83

Synthesis

The synthesis developed by Abdel-Rahman et al.[10] is only one of the many synthetic schemes known for the formation of dihydrotetrazines which can be oxidized to their respective s-tetrazines.[46,47] The synthesis is quite simple in that it involves merely refluxing a mixture of hydrazine hydrate, a nitrile, flowers of sulfur, and ethanol for a period of one to three hours. As an example, use of benzonitrile in the Abdel-Rahman synthesis yields 85% dihydro-3,6-diphenyl-1,2,4,5-tetrazine. Aromatic nitriles generally produce dihydrodiaryltetrazines in high yield, whereas alkyl nitriles give only low yields of the respective dihydrodialkyltetrazines.

Besides being simple, the Abdel-Rahman synthesis represents a route to dihydrotetrazines under non-acidic, non-forcing reaction conditions. Thus, the synthesis is ideal for preparation of the intriguing 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) which can be converted into the equally interesting 3,6-dicyclopropylpyridazine (80) by known routes.[1]

Of itself the Abdel-Rahman synthesis presents an interesting mechanistic problem. While synthesizing large quantities of 3,6-diphenyl-1,2,4,5-tetrazine (1), about a 2.5% isolated yield of the well-known 2,5-diphenyl-1,3,4-thiadiazole (84)[48] was obtained as a side product in this work.

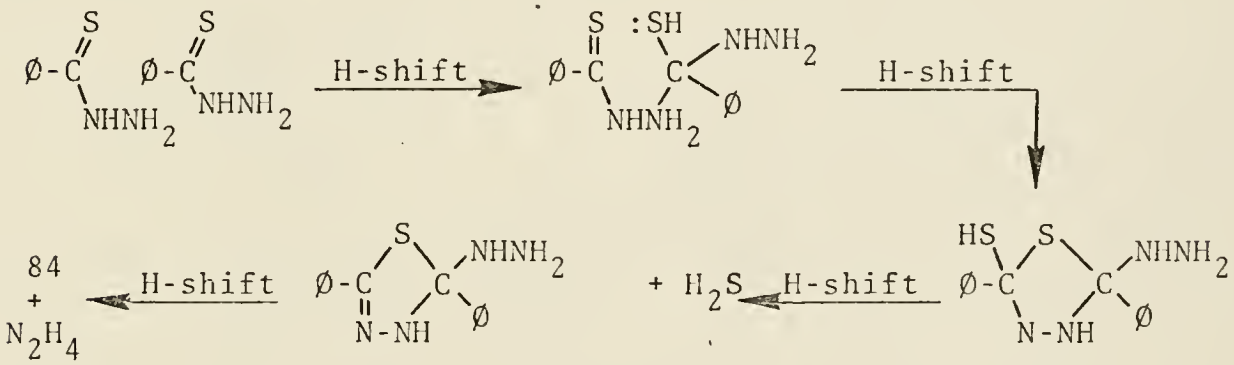


84

No mention of 84 was made by Abdel-Rahman. The only reported work towards enlightening the mechanism of the dihydrotetrazine forming reaction was to ascertain that phenylthiohydrazide, under the reaction conditions, does not afford dihydrodiphenyltetrazine. Abdel-Rahman found that under the reaction conditions employed phenylthiohydrazide reacts to form, not dihydrodiphenyltetrazine, but rather "something else."[10] What the "something else" is was not

determined. No spectral or chemical data on the "something else" were given.

The mechanistic possibilities for the formation of 84 are quite large and, as yet, uninvestigated. One possible mechanism involving phenylthiohydrazide is illustrated in Scheme 21. The freedom of assuming that phenylthiohydrazide can be formed under the reaction conditions has been taken. Phenylthiohydrazide is known to react with phenylimidate ethyl ester hydrochloride in refluxing ethanol[49] and with benzoyl chloride in N-methylpyrrolidinone[50] to form 84.

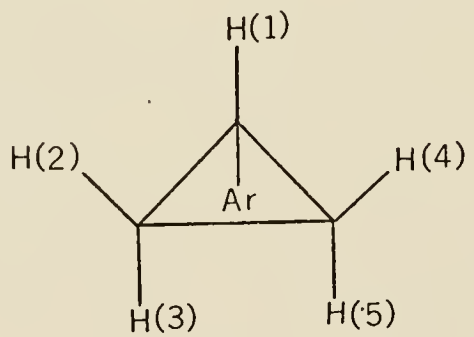


Scheme 21

Using the above-described method of Abdel-Rahman, the desired 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) was synthesized in low yield (5.7% by glpc). The crystalline 79 displayed the expected chemical and spectral properties given in Chapter V.

At ambient temperatures, the NMR spectrum of 79 in deuteriochloroform consisted of two multiplets centered

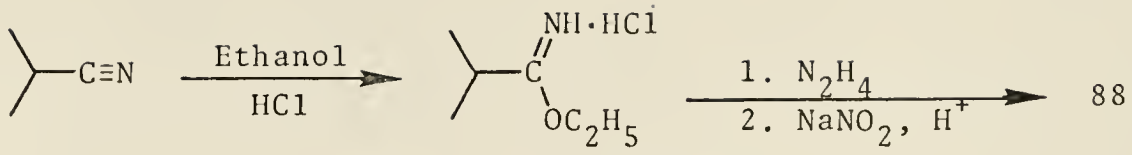
at τ7.47 and 8.73 integrating for two and eight protons respectively as illustrated in Figure 10. Since the chemical shift and coupling constant data could not be determined by casual inspection, the data were obtained by computer analysis by King[51] who used the LAOCOON II program modified for magnetic equivalence (LAMP II). The chemical shift data are reproduced in Table VI along with the data for 3,6-dicyclopropylpyridazine (80). The coupling constant data for 79, 80, and the two known cyclopropyl systems, 85[52] and 86,[53] are given in Table VII. It will be noted that, as expected, the coupling found in systems 79 and 80 is quite similar to that found in the three known systems given in Table VII. The numbering system of structure 87 is used to identify the cyclopropyl protons. Recognizing that 79 and



87

80 can exist in different rotameric forms was not necessary for the computer analysis of 79 or 80.

As a model compound for 79, the known 3,6-di-iso-propyl-1,2,4,5-tetrazine (88)[54] was synthesized by the method of Scheme 22.[55] The spectral properties for 88, which are



Scheme 22

given in Chapter V, agreed with those in the literature.[55]

The previously unknown 3,6-dicyclopropylpyridazine (80) and its model compound 3,6-di-iso-propylpyridazine (89) were both easily synthesized by reaction of respectively, 79 and 88 with norbornadiene.[1] Both crystalline, colorless compounds displayed the expected spectral properties.

In the aromatic region, the NMR spectrum of 89 displayed the expected sharp two-proton singlet at τ2.59 for the pyridazine protons. The iso-propyl groups manifested themselves by the expected septuplet at τ6.75 (J = 7.0 Hz) which integrates for two protons and doublet at 8.65 (J = 7.0 Hz) which integrates for twelve protons. The coupling constants for 89 are the same as in the known tetrazine 88. As was anticipated, the iso-propyl methine protons of 89 appeared at higher field than the corresponding protons of tetrazine 88 (vide infra and Table VIII).

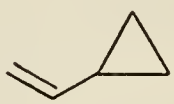
The ambient temperature NMR spectrum of 3,6-dicyclopropylpyridazine (80) in deuteriochloroform is given in Figure 15. The spectrum displays the anticipated two-proton singlet at τ2.92 and, two- and eight-proton multiplets centered at 8.05 and 9.0 respectively.

Table VI

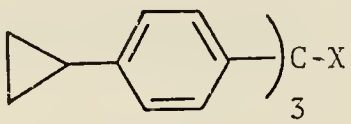
Chemical Shift Data for Tetrazine 79 and Pyridazine 80

Compound	Nucleus	Shift[a]	Standard Deviation (Hz)
79	H(1)	-147.35	0.02
	H(2,4)	-73.23	0.02
	H(3,5)	-76.80	0.02
80	H(1)	-116.99	0.01
	H(2,4)	-56.76	0.01
	H(3,5)	-63.77	0.01

[a]In Hz downfield from TMS as internal standard using carbon disulfide as a solvent.



85



86a X = OH
b X = +

Table VII

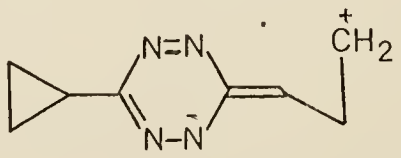
Magnetic Coupling Data for 79, 80, 85 and 86

Compound	Nuclei	Coupling Constant (Hz)	Standard Deviation (Hz)
79	1-2, 1-4	8.30	0.03
	1-3, 1-5	4.86	0.03
	2-3, 4-5	-4.1	0.2
	2-4	9.1	0.6
	2-5, 3-4	6.8	0.2
	3-5	9.7	0.6
80	1-2, 1-4	8.25	0.01
	1-3, 1-5	4.83	0.01
	2-3, 4-5	-3.95	0.02
	2-4	9.2	0.1
	2-5, 3-4	6.48	0.02
	3-5	9.4	0.1
85[52]	1-2, 1-4	8.16	----[a]
	1-3, 1-5	4.89	----
	2-3, 4-5	-4.49	----
	2-4	9.02	----
	2-5, 3-4	6.22	----
	3-5		
86a[53]	1-2, 1-4	8.40	----[a]
	1-3, 1-5	5.05	----
	2-3, 4-5	-4.48	----
	2-4	9.31	----
	2-5, 3-4	6.31	----
	3-5	9.36	----
86b[53]	1-2, 1-4	8.25	----[a]
	1-3, 1-5	4.80	----
	2-3, 4-5	-4.88	----
	2-4	9.05	----
	2-5, 3-4	6.89	----
	3-5	9.78	----

[a]No standard deviation given.

Dicyclopropyltetrazine and Dicyclopropylpyridazine. - The Ground State

If the cyclopropyl rings of tetrazine 79 and pyridazine 80 are conjugated with the heteroaromatic rings in the ground states of these molecules, several phenomena should be observable. Since cyclopropyl conjugation with the heteroaromatic ring can occur only in the bisected conformation (vide supra), the methine hydrogen of the cyclopropyl ring should spend more of its time in the deshielding region of the heteroaromatic ring than it would if the cyclopropyl ring was able to rotate freely. Thus, the methine proton should be deshielded relative to freely rotating systems such as the iso-propyl compounds 88 and 89, excluding the effects of the groups themselves. The cyclopropyl rings of 79 and 80 should conjugate with the heteroaromatic rings via such resonance structures as 90. Thus, the methylene protons of the cyclopropyl rings should show deshielding due to the charge which is placed on the β-carbons of the cyclopropyl ring. Lowering the temperature of a solution of either 79 or 80 should increase the number of molecules in the bisected configuration while raising the temperature should decrease the number of molecules in the bisected configuration.



90

As illustrated in Figures 11-13, lowering the temperature of a solution of 79 in deuteriochloroform changes the NMR spectrum of 79 drastically. At -60° the lower field multiplet appears as what is essentially a pentet at τ7.35 (J = 6.6 Hz) and the higher field multiplet shows up as a doublet at 8.62 (J = 6.6 Hz). The temperature-dependent spectral changes have been interpreted as being due to H(2)-H(5) becoming magnetically equivalent thus simplifying the spectrum.[51] It will be noted that the chemical shift of the methine protons only changes from τ7.54 to 7.37 or 0.17 ppm - a shift in the right direction for increased cyclopropyl conjugation but a shift whose magnitude may be accounted for by changes in solute-solvent interactions. The simplification of the NMR spectrum of 79 on lowering the temperature of its deuteriochloroform solution is consistant with increased cyclopropyl conjugation only if it is assumed that the equivalence of H(2)-H(5) is due only to increased population of the bisected conformation. Again the simplification of the NMR spectrum may be accounted for by assuming changes in solvent-solute interactions.

An NMR spectrum of 79 in diphenyl ether is given in Figure 14. Although the shape of the multiplets has changed, the multiplets are still due to the methine and methylene protons. Heating a solution of 79 in diphenyl ether causes no change in the NMR spectrum. Especially notable is the fact that the chemical shift of the methine proton is essentially unchanged on heating.

Figures 15-17 illustrate that the cyclopropyl multiplets in the NMR spectrum of 80 are even less affected than the multiplets of a spectrum of 79 on lowering the temperature of a solution of 80. If the simplification of the NMR spectrum of 79 was due to cyclopropyl conjugation (vide supra), the fact that simplification of the NMR spectrum of 80 is less pronounced than in the case of 79 is completely in accord with the supposition that cyclopropyl conjugation in pyridazine 80 will be less than in tetrazine 79 (vide supra).

Of interest in the NMR spectra of 80 and its model compound 3,6-di-iso-propylpyridazine (89) are the pyridazine protons. The aromatic protons of the cyclopropyl compound 80 are shielded relative to the aromatic protons of the iso-propyl compound 89 by 0.33 ppm. The shielding of the aromatic protons of 80 may be attributed to either shielding by the cyclopropyl rings in the bisected conformation when one or both of the cyclopropyl rings is syn to the aromatic proton or the aromatic protons may be shielded simply due to electronic density flowing into the pyridazine ring from the cyclopropyl rings. It is certainly true that the cyclopropyl rings exert an electron-withdrawing effect inductively,[56] but the resonance effect of cyclopropyl is positive and the positive resonance effect should overcome the negative inductive effect. Either of the above effects which cause the aromatic protons of 80 to be shielded relative to the protons

Figure 10. NMR spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in $CDCl_3$ at NMR probe temperature (40°)

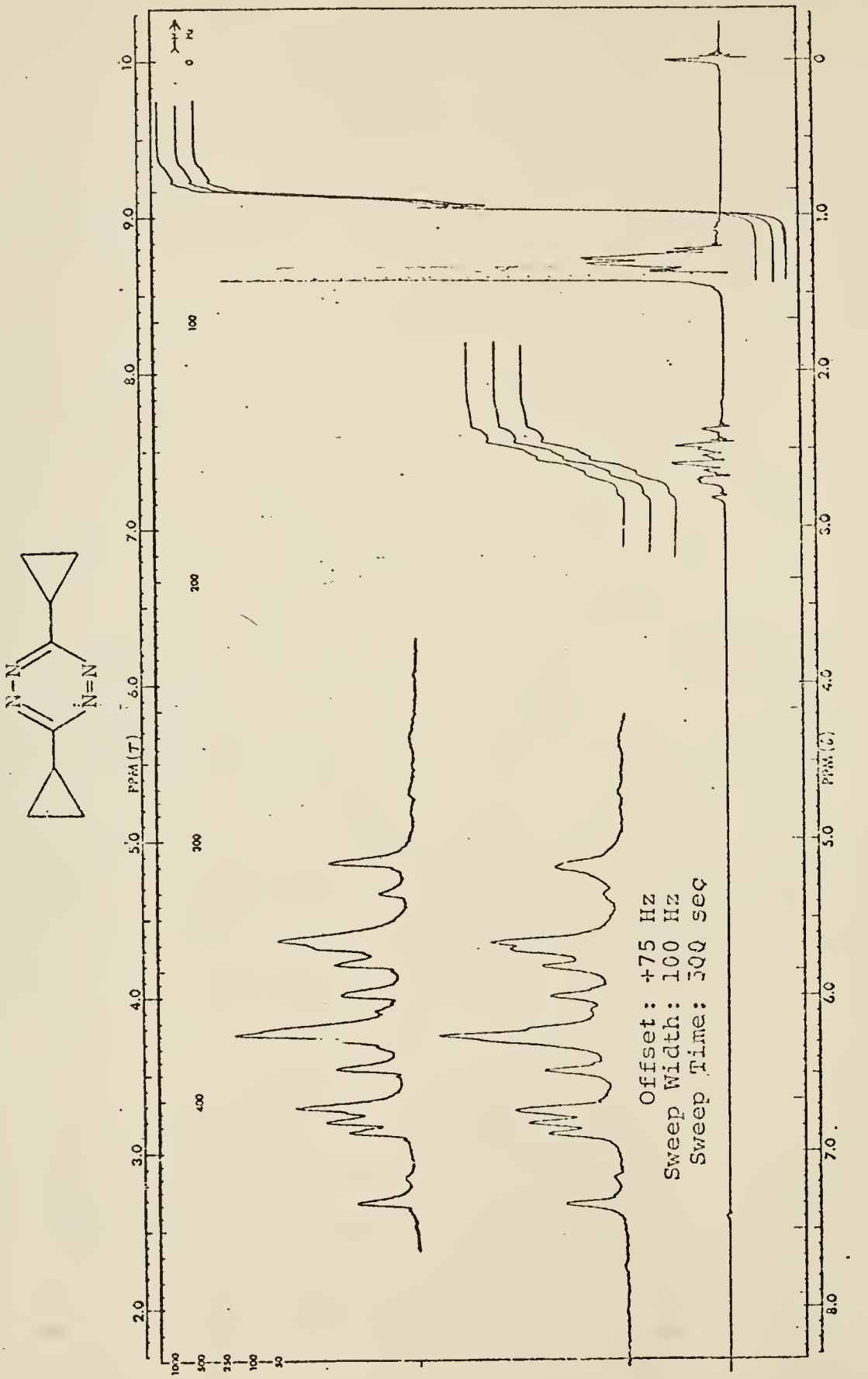

Offset: +75 Hz
Sweep Width: 100 Hz
Sweep Time: 300 sec
PPM (τ)
PPM (δ)

Figure 11. NMR spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in $CDCl_3$ at -10°

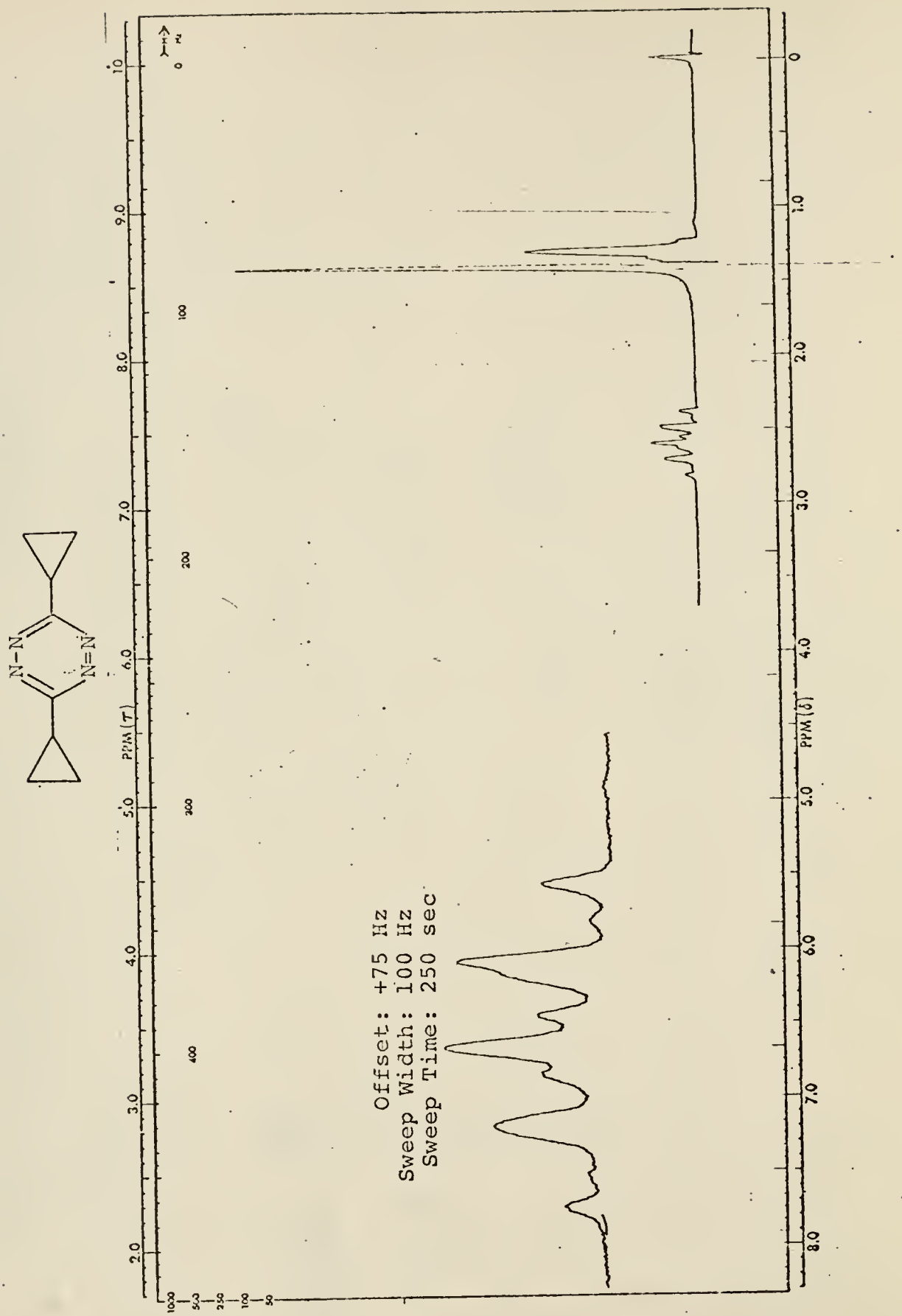

Offset: +75 Hz
Sweep Width: 100 Hz
Sweep Time: 250 sec
PPM(τ)
PPM(δ)
N-N
N=N

Figure 12. NMR spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in $CDCl_3$ at -30°

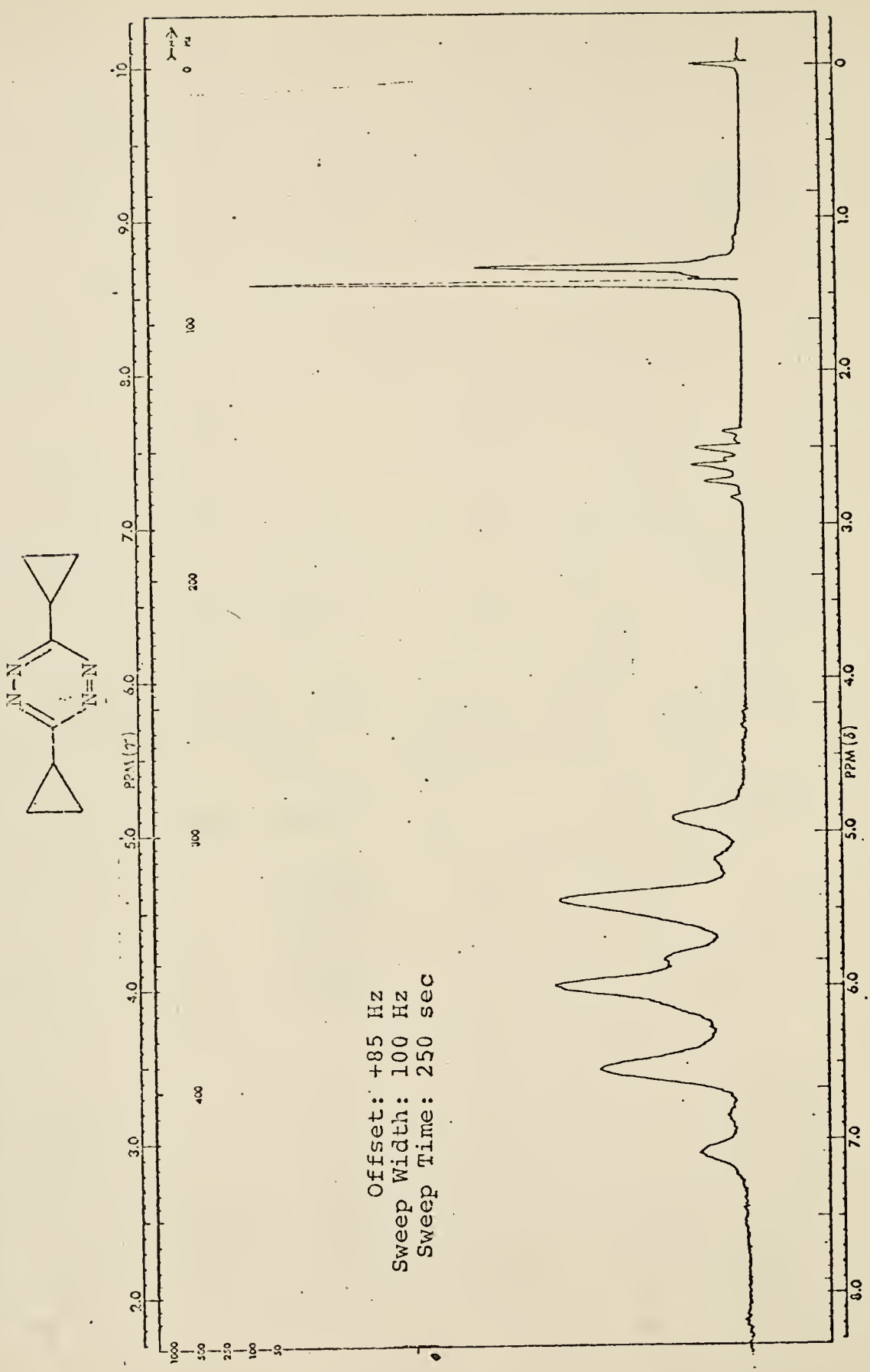

Offset: +85 Hz
Sweep Width: 100 Hz
Sweep Time: 250 sec
PPM (τ)
PPM (δ)
N-N
N=N

Figure 13. NMR spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in $CDCl_3$ at -60°

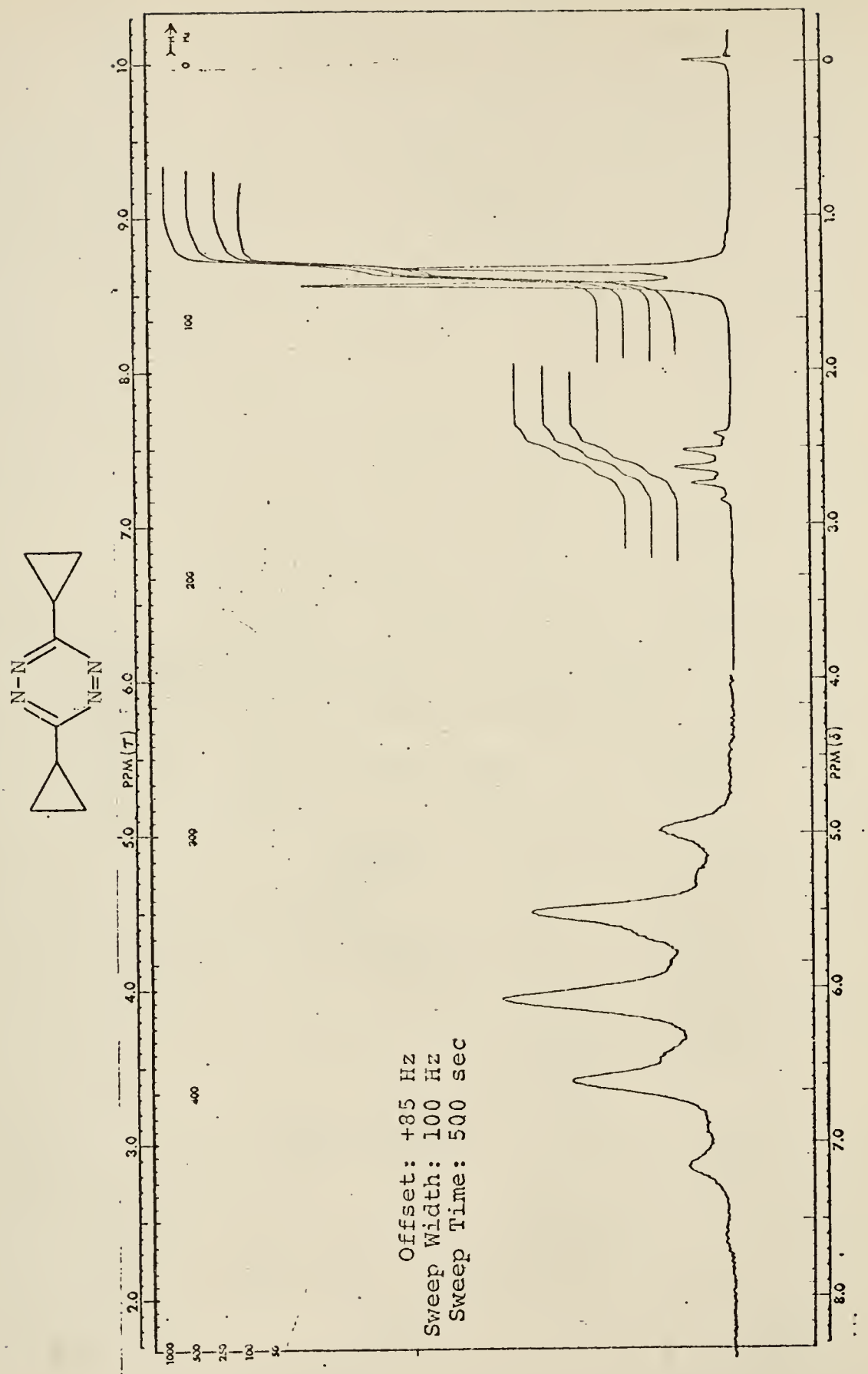
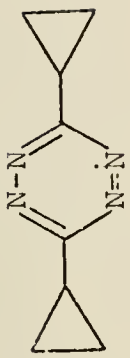

N-N
N=N
Offset: +85 Hz
Sweep Width: 100 Hz
Sweep Time: 500 sec
PPM(τ)
PPM(δ)

Figure 14. NMR spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in diphenyl ether at NMR probe temperature (40°)


N-N
N=N

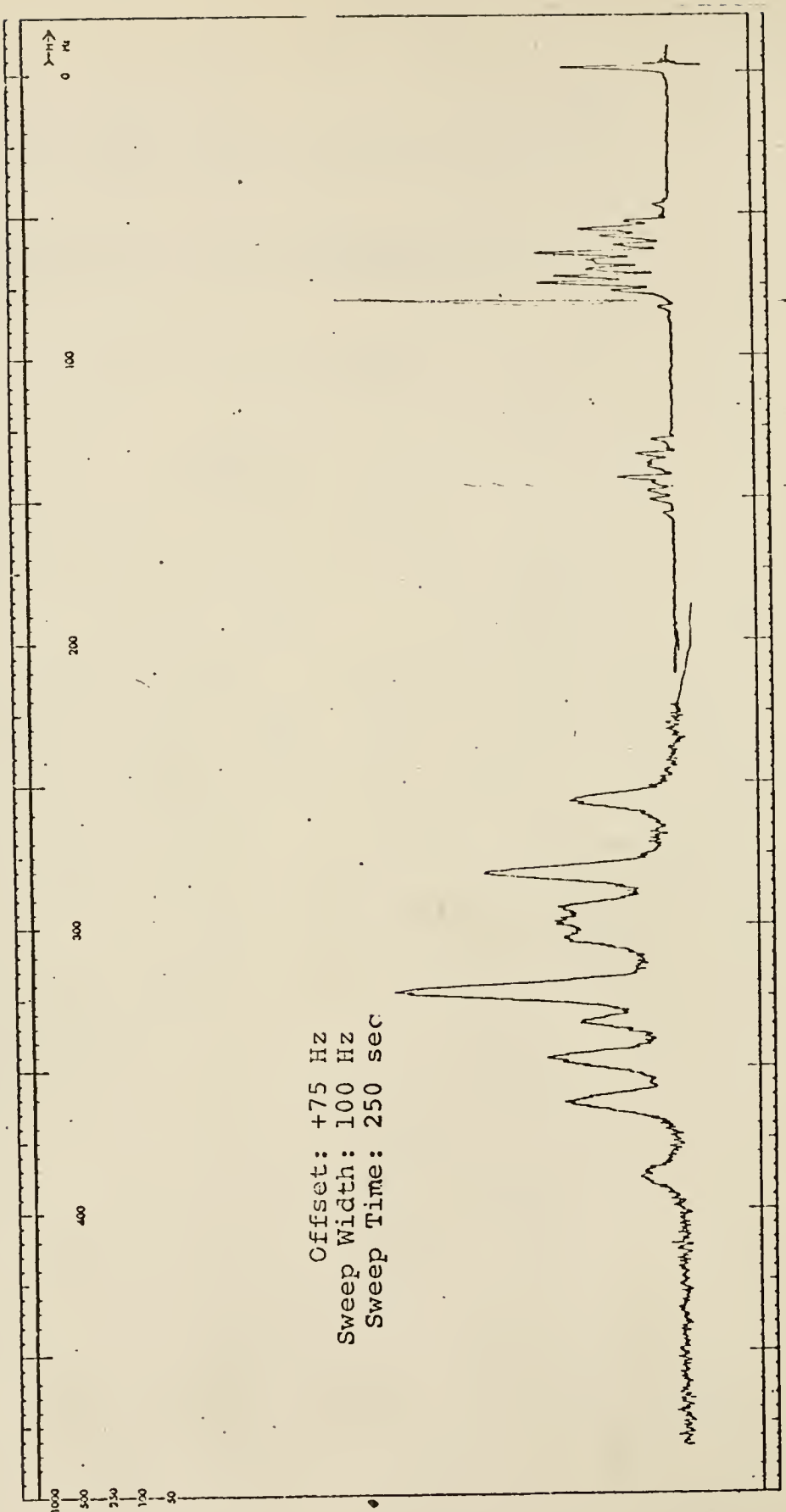

Offset: +75 Hz
Sweep Width: 100 Hz
Sweep Time: 250 sec
0
100
200
300
400
1000
500
250
125
50

Figure 15. NMR spectrum of 3,6-dicyclopropylpyridazine (80) in $CDCl_3$ at 42.5°

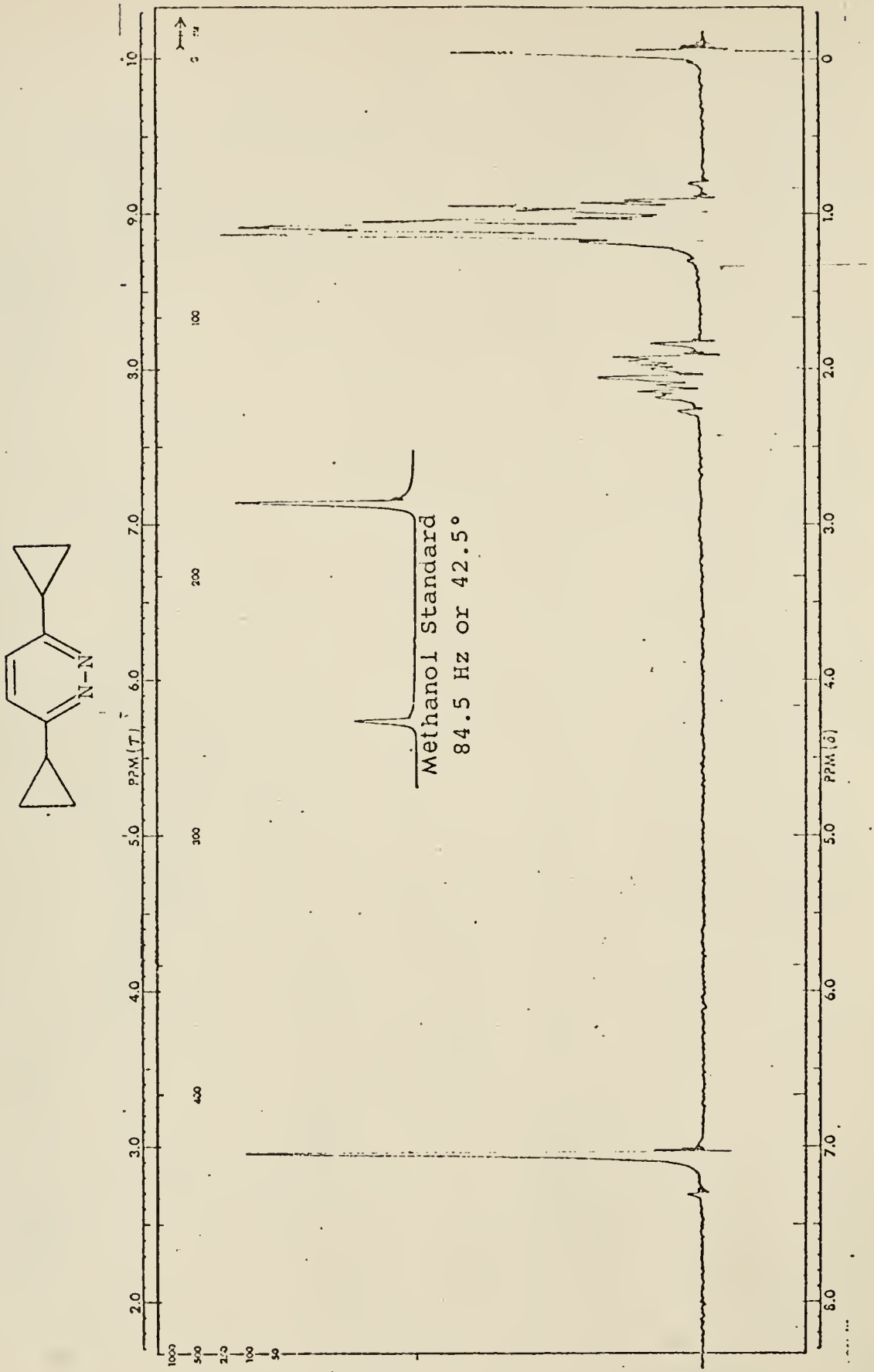
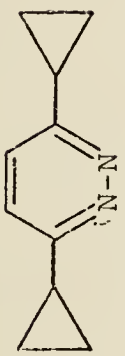

Methanol Standard
84.5 Hz or 42.5°
PPM(τ)
PPM(δ)

Figure 16. NMR spectrum of 3,6-dicyclopropylpyridazine (80) in $CDCl_3$ at -5.5°



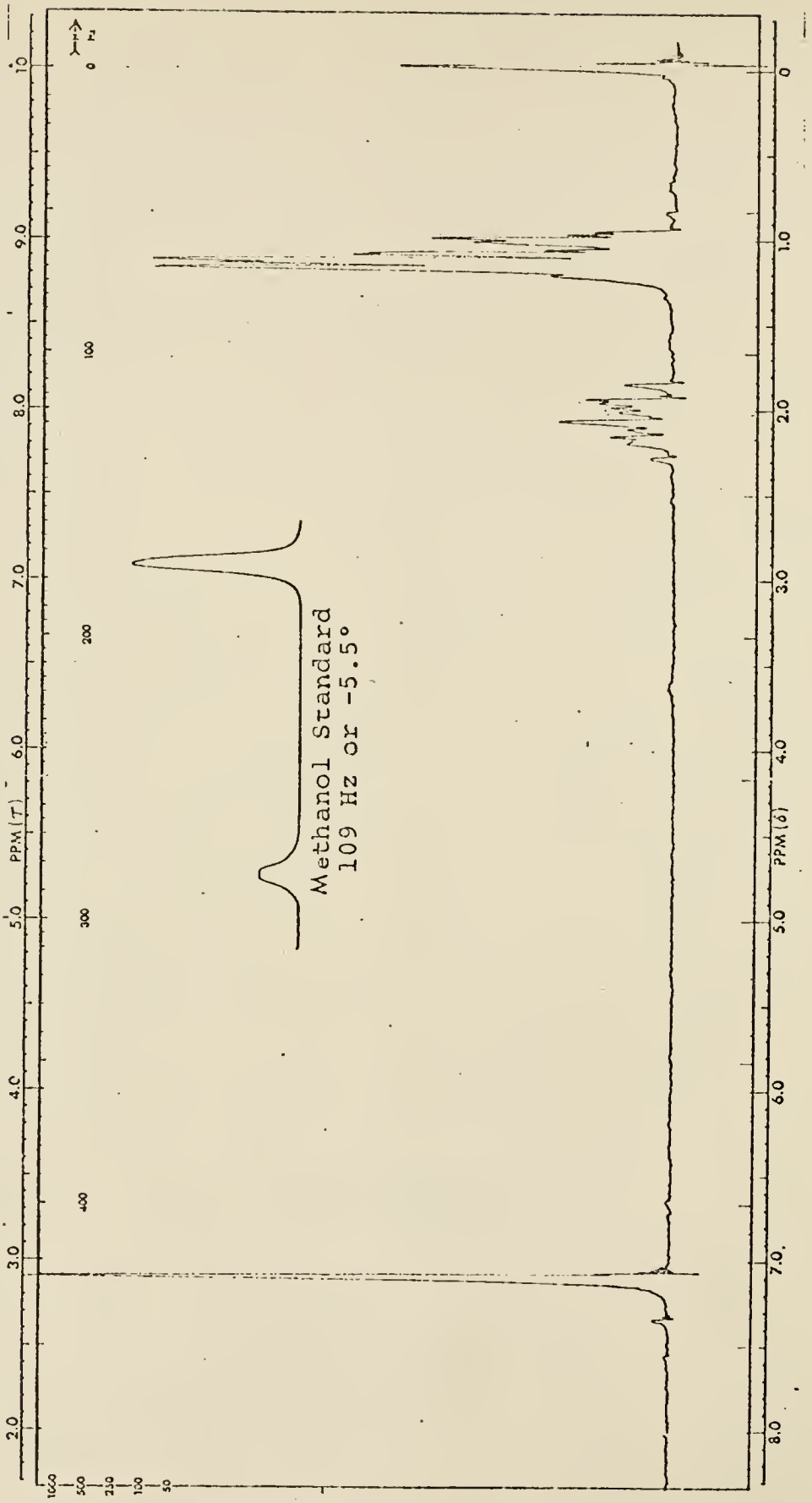
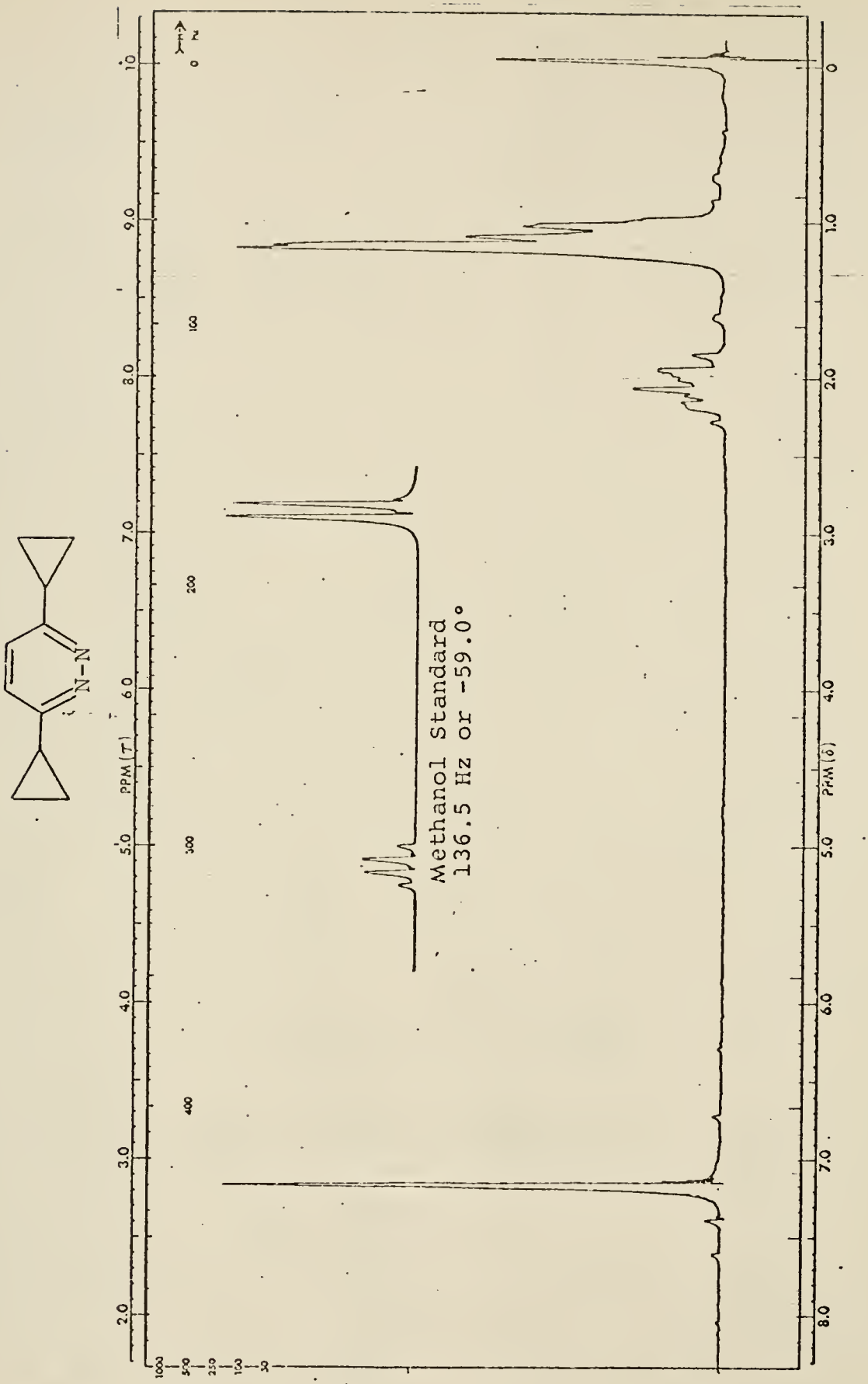

Methanol Standard
109 Hz or -5.5°
PPM(τ)
PPM(δ)

Figure 17. NMR spectrum of 3,6-dicyclopropylpyridazine (80) in $CDCl_3$ at -59.0°


Methanol Standard
136.5 Hz or -59.0°
PPM(τ)
PPM(δ)
N-N

of 89 requires that the cyclopropyl rings of 80 be in the bisected conformation.

Lowering the temperature of a solution of 80 actually causes the aromatic protons of 80 to become more deshielded rather than more shielded. This is in complete accord with 80 assuming a conformation such as 83 in which the aromatic protons are no longer in the shielding region of the cyclopropyl rings. Again the deshielding of the aromatic protons may be accounted for by assuming changes in solvent-solute interactions with decreasing temperature.

Examination of the NMR spectrum of the three iso-propyl compounds 88, 89, and 1,4-di-iso-propylbenzene (91)[57] reveals that, as anticipated, on transforming from the carbocyclic 91 to the diazine 89 to the tetrazine 88, a downfield shift is experienced by both the methine and methyl protons of the iso-propyl groups. The shift difference (see Table VIII) on exchange of two C-H moieties for nitrogens is about 0.30 to 0.47 ppm for the methine protons while the shift difference for the methyl protons is only about 0.15 ppm. Since, with the exception of a very small hyperconjugative effect, the iso-propyl groups can be assumed to be freely rotating, the above shift differences can be attributed largely to inductive effects produced by the nitrogens which are more electron-withdrawing than the C-H units.

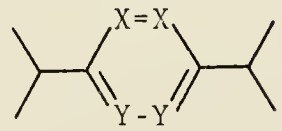
Examination of the three cyclopropyl compounds 79, 80, and monocyclopropylbenzene (92)[58] reveals the same type of downfield shift trend as with the iso-propyl compounds above.

However, it will first be noted that the shift differences for the cyclopropyl methine proton are not as great as in the iso-propyl series. This anomalous behavior cannot be explained readily. The important protons in this series are the ones β to the aromatic ring. The fact that these β-methylene protons show increased deshielding relative to the methyl protons in the iso-propyl series is a good indication that positive charge is being placed on the β-carbons via resonance structures such as 90 which is a good indication that the cyclopropyl rings of 79 and 80 are conjugating with the heteroaromatic ring and providing it with electron density.

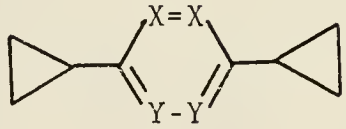
That monocyclopropylbenzene is as valid a model as 1,4-dicyclopropylbenzene can be shown in two ways. First, a visual examination of an NMR spectrum of an impure sample of dicyclopropylbenzene[59] shows that the chemical shift of the methine proton is at about the same shift as the methine of monocyclopropylbenzene. In both cases the center of the methine proton multiplet is taken as a good first approximation of the chemical shift of the methine proton. The NMR spectra of the known 2-cyclopropylthiophene and 2,5-dicyclopropylthiophene have been reported.[60] Using the above-described center-of-the-multiplet approach, one finds that the methine proton of 2,5-dicyclopropylthiophene is actually at lower field than the methine proton of the monocyclopropylthiophene.

Table VIII

Chemical Shift Data for iso-Propyl and Cyclopropyl Aromatic Compounds



Compound	$\tau_{methine}$	$\Delta\tau$	τ_{CH_3}	$\Delta\tau$
X = Y = CH[a,b]	7.19	0.47	8.79	0.15
X = CH, Y = N[c]	6.72	0.30	8.64	0.16
X = Y = N[c]	6.42		8.48	



Compound	$\tau_{methine}$	$\Delta\tau$	τ_{CH_a}	$\Delta\tau_a$	τ_{CH_b}	$\Delta\tau_b$
X = Y = CH[a,d,e]	8.20	0.15	9.32	0.27	9.26	0.32
X = CH, Y = N[c]	8.05	0.51	9.05	0.28	8.94	0.22
X = Y = N[c]	7.54		8.78		8.72	

[a]No solvent given. [b]Ref. 56. [c]In carbon disulfide. [d]Mono cyclopropyl rather than dicyclopropyl. See text. [e]Ref. 57.

Dicyclopropyltetrazine and Dicyclopropylpyridazine - The Excited State

After ascertaining that some cyclopropyl conjugation is present in the ground states of tetrazine 79 and pyridazine 80, it was of interest to examine the possibility of cyclopropyl conjugation in the excited states of these molecules. First, however, a discussion of the electronic spectra of tetrazine, pyridazine, and their simple derivatives is in order.

Being heteroaromatics tetrazines and pyridazines show both $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ transitions in their electronic spectra. The lowest energy $n\rightarrow\pi^*$ transition of tetrazines is of such low energy that it occurs in the visible region of the spectrum imparting a purple color to tetrazines. Since pyridazines have no absorptions in the visible region, they are colorless.

Table IX lists the absorbances for s-tetrazine and some of its simple alkyl and aryl derivatives. Table X lists the absorbances for pyridazine and its known aliphatic and aryl derivatives.

As expected, the position of the $n\rightarrow\pi^*$ transition in dicyclopropyltetrazine 79 is hypsochromically shifted with respect to other alkyl tetrazines due to the relative electron-withdrawing power of cyclopropyl relative to "normal" alkyl groups.[56] The $n\rightarrow\pi^*$ band of both 79 and 88 shifts hypsochromically on changing from a nonpolar solvent (cyclohexane) to a polar solvent (ethanol) as expected.[61]

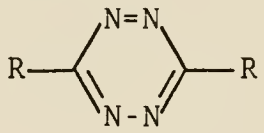
The bands assigned as secondary π→π* absorbances (^1L_b) in both 79 and 88 shifted bathochromically on changing from cyclohexane to ethanol as expected.[61] Replacement of the iso-propyl groups of 88 with cyclopropyl groups shifts the secondary (^1L_b) band of 88 bathochromically by 41 nm in ethanol and 39 nm in cyclohexane.

Also the UV spectrum of 79 contains at shorter wavelengths a new band that does not appear in the spectra of any other alkyl tetrazines. Although this band does not show the expected shift on solvent change, it is assigned as the primary π→π* band (^1L_a) of the aromatic tetrazine ring. This primary π→π* band would be the band predicted by Nishimoto[62] to be at 191 nm for s-tetrazine. The only UV absorbance displayed by 3,6-diphenyl-1,2,4,5-tetrazine (1) is assumed to be this (^1L_a) band on the basis of its intensity. It is also assumed that the (^1L_b) band of 1 is masked by the intense (^1L_a) band.

On comparing 79 and 88, the bathochromic shift of the secondary π→π* band and the appearance of the previously unobserved (in the alkyl series) primary π→π* band, due to a bathochromic shift of that band, is unambiguous evidence for cyclopropyl conjugation in the excited state. It will be noted that in ethanol the (^1L_a) band of 79 is at 222 nm while in 1 the same band is at 297 nm which is in accord with the known pattern of phenyl causing greater bathochromic shifts than cyclopropyl which in turn causes a bathochromic shift from the alkyl substituted compound.

Table IX

Principal Absorbances for Some Tetrazines[a]

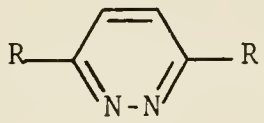


R	Solvent	n→π* (nm)	π→π* (nm)
H[b]	cyclohexane	542 (829)	252 (2150)
		320 (26)	
CH_3[c]	ethanol	538 (560)	274 (3620)
CH_3[b]	cyclohexane	562 (832)	273 (3720)
C_2H_5[c]	ethanol	540 (500)	273 (3190)
C_3H_7[c]	ethanol	542 (470)	275 (2940)
iso-C_3H_7[c]	ethanol	545 (470)	273 (3050)
iso-C_3H_7[d]	ethanol	544 (460)	273 (2920)
	cyclohexane	552 (537)	271 (3020)
$C_{11}H_{23}$[c]	ethanol	542 (535)	276 (3070)
C_3H_5[d]	ethanol	537 (502)	314 (1780)
		270 (505)	222 (20100)
	cyclohexane	543 (758)	310 (1950)
		274 (s, 619)	226 (21700)
C_6H_5[e]	chloroform	545 (500)	300 (60000)
C_6H_5[d]	ethanol	546 (449)	297 (35700)

[a]See Chapter V for complete spectra of all compounds recorded in this work i.e. shoulders and inflections. Also see Figures 18-21 for reproductions of the spectra of the cyclopropyl compound 79. [b]Ref. 63. [c]Ref. 54. [d]This work. [e]Ref. 64.

Table X

Principal Absorbances for Some Pyridazines[a]



R	Solvent	n→π* (nm)	π→π* (nm)
H[b]	ethanol	313 (303)	246 (1160)
	cyclohexane	340 (315)	246 (1300)
iso-C_3H_7[c]	ethanol	320 (227)	257 (1650)
	cyclohexane	344 (290)	262 (1670)
C_3H_5[c]	ethanol	317 (s, 248)	278 (1550)
			226 (13400)
	cyclohexane	342 (299)	276 (1330)
			225 (14800)
C_6H_5[c]	ethanol		279 (29300)

[a]See Chapter V for complete spectra of compounds recorded in this work i.e. shoulders and inflections. See also Figures 22 and 23 for reproductions of the spectra of the cyclopropyl compound 80. [b]Ref. 63. [c]This work.

In the pyridazine series again the absorbance assigned to the n→π* transition shifts hypsochromically on changing the solvent from cyclohexane to ethanol for 80 and 89. Also the position of the n→π* absorbance for the cyclopropyl derivative, 80, is at shorter wavelength than the corresponding band for the iso-propyl compound, 89, in accord with the greater inductive effect of the cyclopropyl rings.

As in the case of the tetrazine series the bands assigned to $\pi \rightarrow \pi^*$ transitions shift bathochromically on changing from a nonpolar solvent to a polar one. Again replacement of the iso-propyl groups by cyclopropyl rings causes a large bathochromic shift in the original $\pi \rightarrow \pi^*$ band (secondary or ^1L_b band) and the appearance of a new, more intense $\pi \rightarrow \pi^*$ band (primary or ^1L_a band). The results are again interpreted as evidence for cyclopropyl conjugation in the excited state. It will be noted that, as in the tetrazine series, the (^1L_a) band of the cyclopropyl compound 80 lies above the assumed position for the same band in the iso-propyl compound 89 but below the position of the same band for 3,6-diphenylpyridazine (93).

On comparing tetrazine 79 and pyridazine 80, it would appear that cyclopropyl conjugation is less important in 80 than in 79 in the excited state of these molecules as was anticipated. Using iso-propyl compounds 88 and 89 as model compounds, it can be seen that the shift difference between 79 and 88 is not the same as the shift difference between 80 and 89. The shift difference between the secondary bands of tetrazines 79 and 88 is approximately 40 nm while the corresponding shift difference between the pyridazines 80 and 89 is only about 14 to 21 nm. The results are those anticipated in view of the results in the hydrocarbon series.[45]

No comparison using the primary (^1L_a) bands of 79 and 80 is possible as the position of the primary band in the

corresponding iso-propyl compounds is in the far ultra-violet and could not be determined.

Figure 18. Visible spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in ethanol

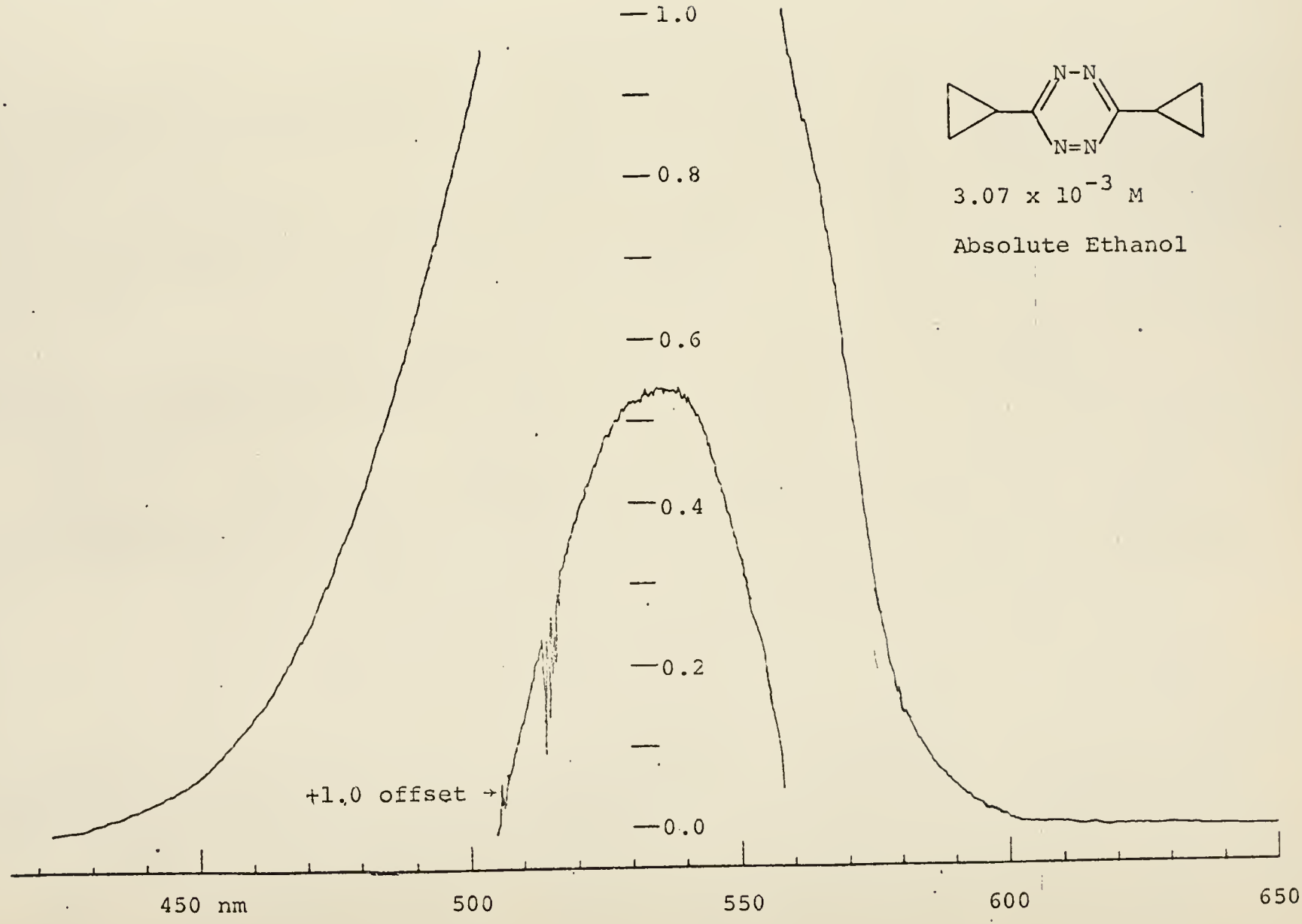

1.0
0.8
0.6
0.4
0.2
0.0
+1.0 offset
450 nm
500
550
600
650
N-N
N=N
3.07 x 10^-3 M
Absolute Ethanol

Figure 19. Visible spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in cyclohexane

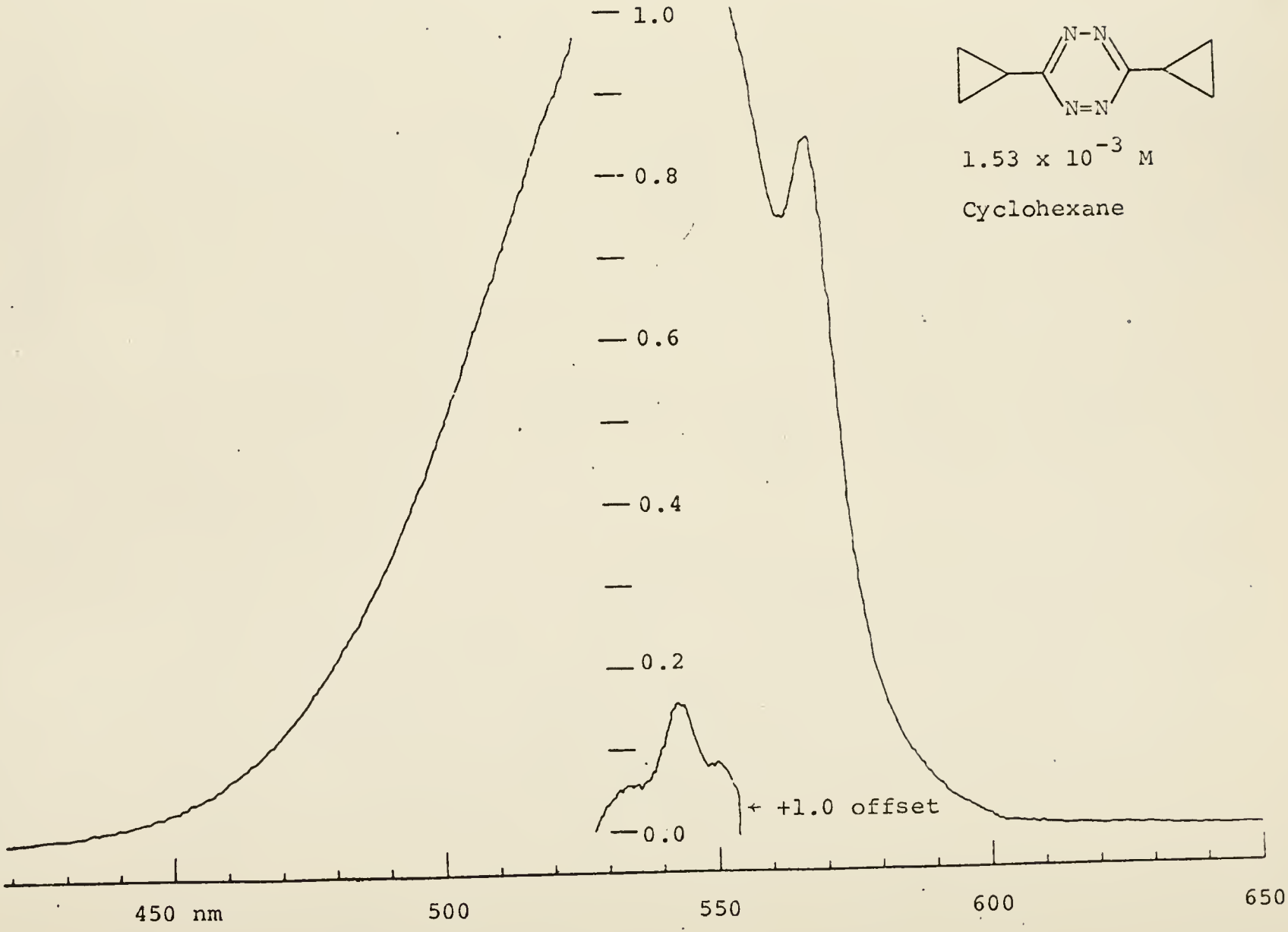

1.0
0.8
0.6
0.4
0.2
0.0
+1.0 offset
450 nm
500
550
600
650
N-N
N=N
1.53 x 10^-3 M
Cyclohexane

Figure 20. UV spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in ethanol

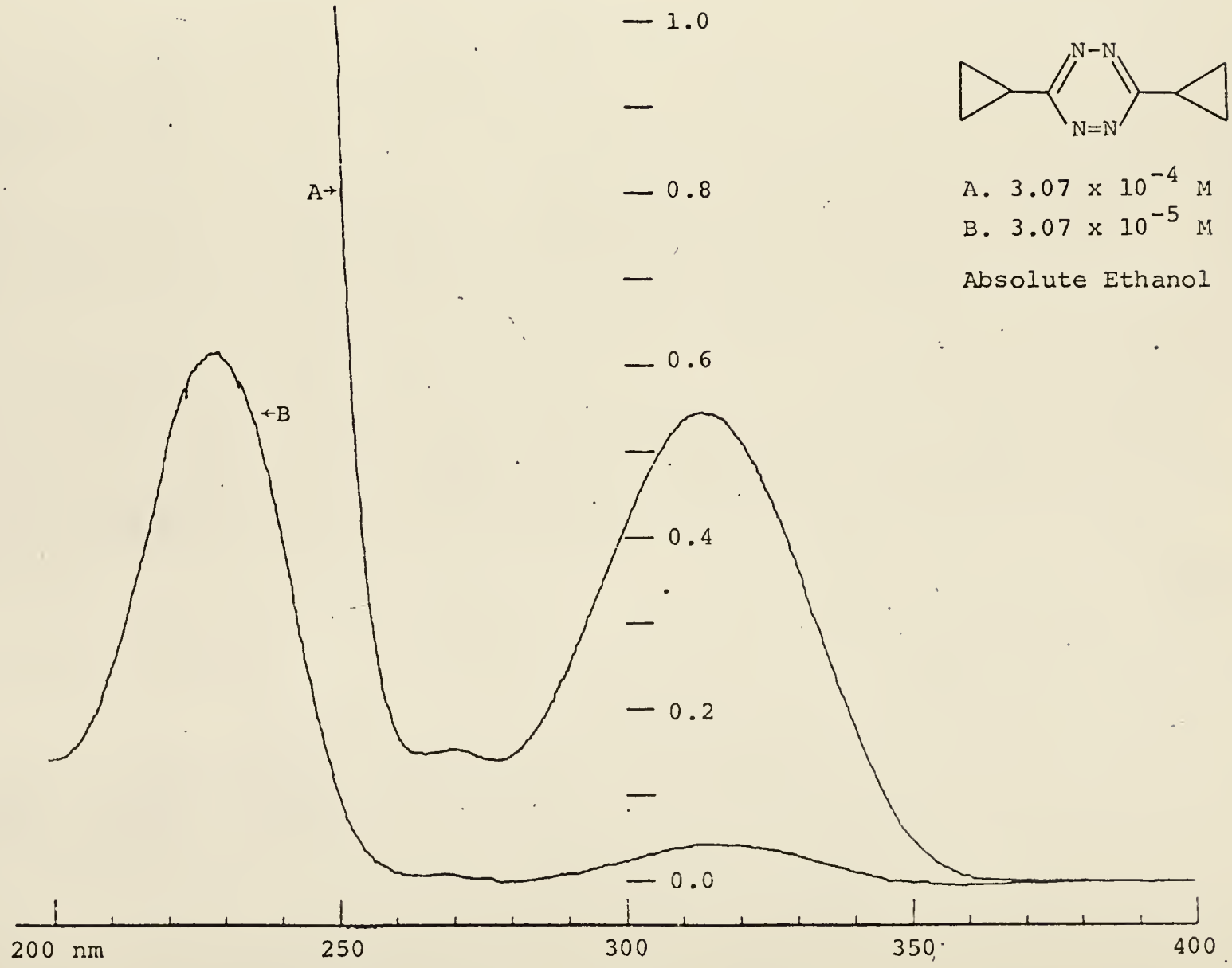

1.0
0.8
0.6
0.4
0.2
0.0
A→
←B
200 nm
250
300
350
400
N-N
N=N
A. 3.07 x 10^-4 M
B. 3.07 x 10^-5 M
Absolute Ethanol

Figure 21. UV spectrum of 3,6-dicyclopropyl-1,2,4,5-tetrazine (79) in cyclohexane

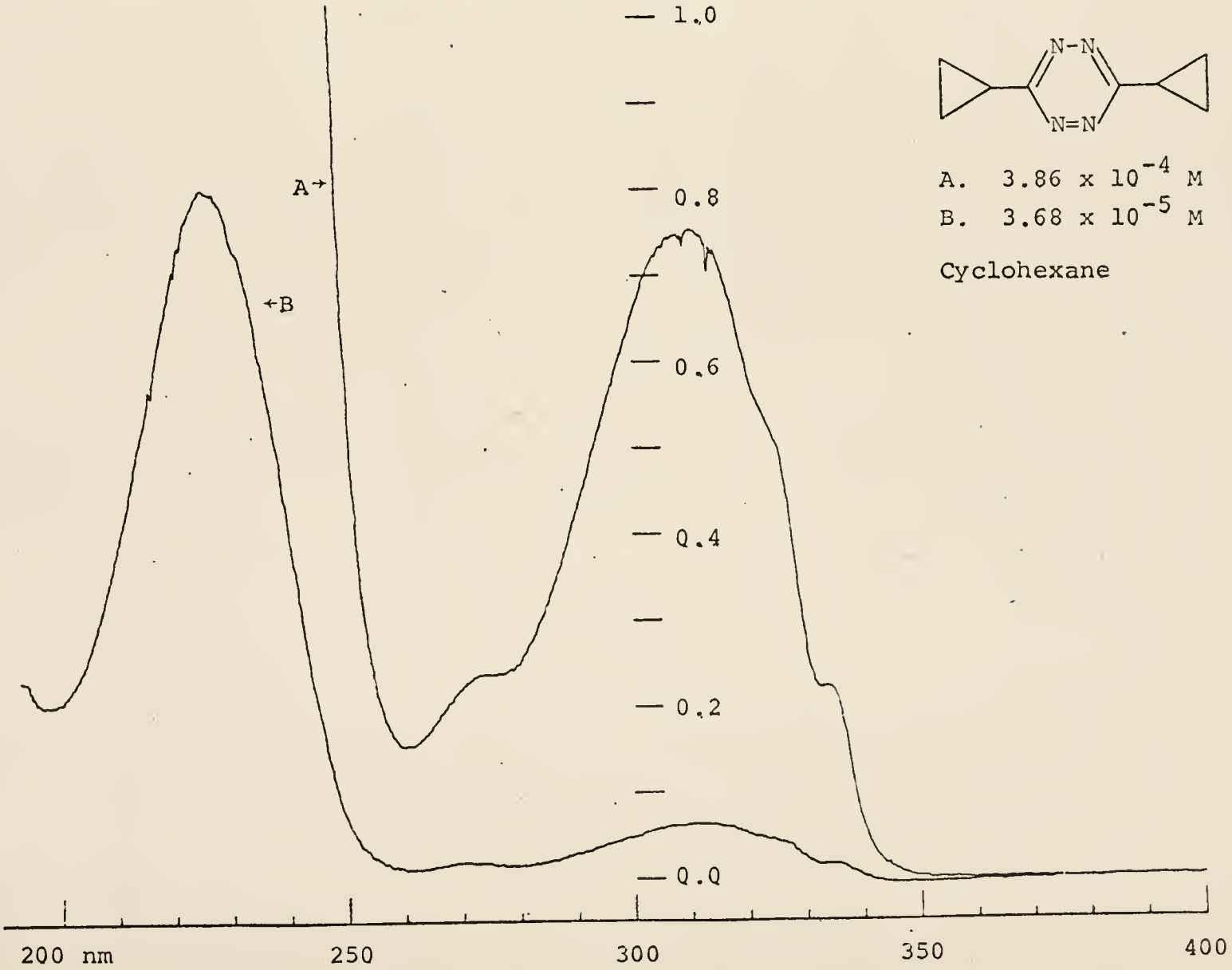
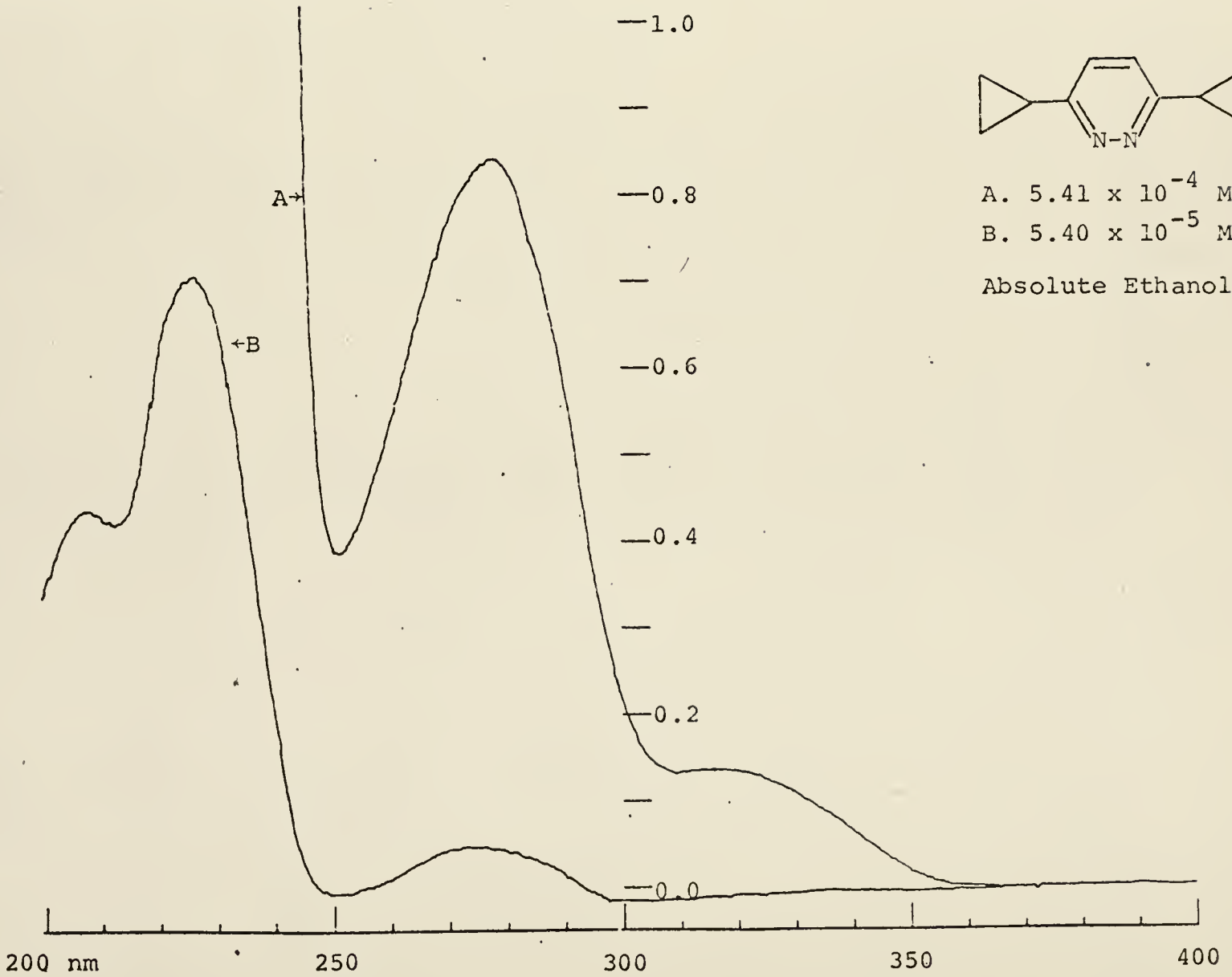

1.0
0.8
0.6
0.4
0.2
0.0
A→
←B
200 nm
250
300
350
400
N-N
N=N
A. 3.86 x 10^-4 M
B. 3.68 x 10^-5 M
Cyclohexane

Figure 22. UV spectrum of 3,6-dicyclopropylpyridazine (80) in ethanol

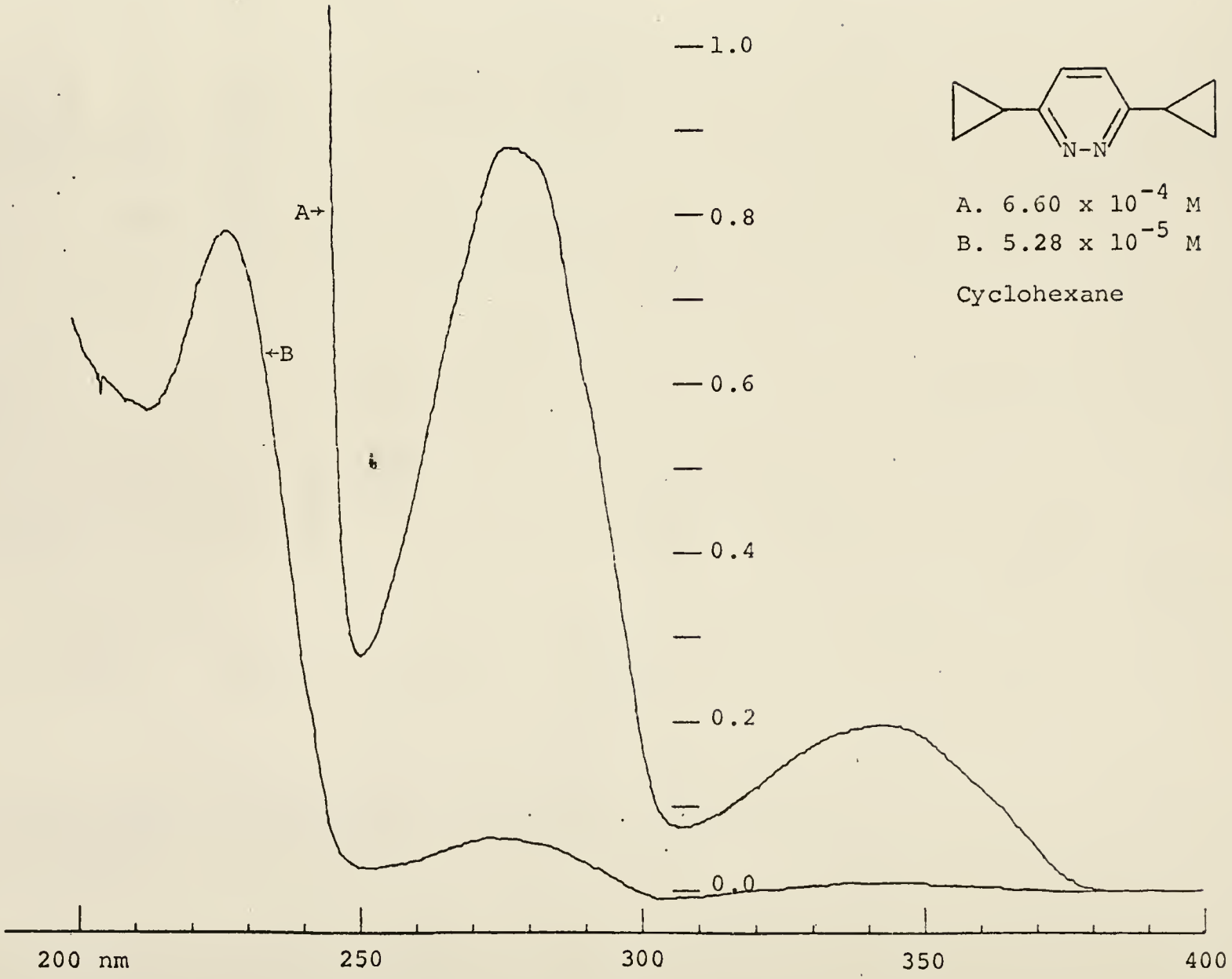


A. 5.41×10^{-4} M

B. 5.40×10^{-5} M

Absolute Ethanol

Figure 23. UV spectrum of 3,6-dicyclopropylpyridazine (80) in cyclohexane


1.0
0.8
0.6
0.4
0.2
0.0
A→
←B
N-N
A. 6.60 x 10^-4 M
B. 5.28 x 10^-5 M
Cyclohexane
200 nm
250
300
350
400

CHAPTER IV

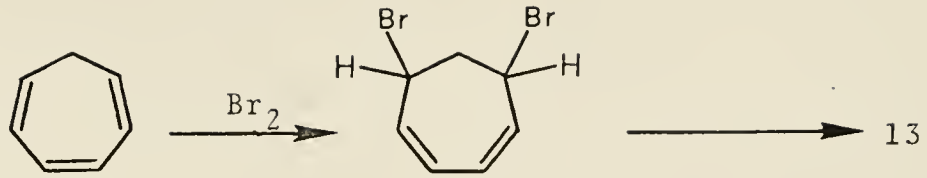
THE DIAZATROPYLIUM CATION AND DIAZATROPONE

As was mentioned in Chapter II, 13 is base peak in the mass spectrum of cycloheptatriene whereas cations similar to 75 are only a few percent of base peak in the mass spectra of 4H-1,2-diazepines and 3,4-diazanorcaradienes. Again the mass spectral behavior of diazanorcaradienes and diazepines appears to have a strong bearing on the chemistry of these heterocycles as will be demonstrated by the results of this chapter.

Attempted Syntheses of 1,2-Diazatropylium Cations

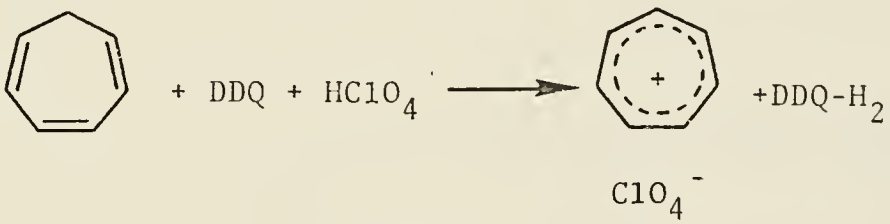
There are several varied methods for producing the carbocyclic tropylium cation.[7,8] Only those methods of direct application to the synthesis of a diazatropylium cation will be reviewed briefly here.

In 1954 Doering and Knox[65] established that the addition of one mole of bromine to cycloheptatriene yielded a dibromide which on heating underwent dehydrohalogenation to yield 15 (bromide gegenion) as illustrated in Scheme 23,



Scheme 23

The oxidizing agent DDQ is known mechanistically to operate primarily as a hyride abstractor.[66] Reid et al.[67] utilized the above fact in synthesizing tropylium perchlorate as depicted in Scheme 24.



Scheme 24

Dauben[68] first reported the use of trityl carbonium ion salts as hydride abstractors in the synthesis of a series of tropylium perchlorates, fluoroborates, bromides, chlorides, and iodides. The other reaction product is triphenylmethane which is readily soluble in diethyl ether and easily removed from the ionic, insoluble tropylium salt by extraction.

On heating, the diazanorcaradiene 6 rapidly undergoes ring inversion presumably via the open 5H-diazepine form.[2,3] It was assumed that on refluxing in benzene enough of this open form would be present to react with DDQ to form 3,7-diphenyl-1,2-diazatropylium cation whose gegenion, the DDQ-H

anion, could be exchanged for the more suitable perchlorate anion.

Mixing DDQ and 6 at room temperature in benzene causes an immediate color change from bright yellow to dark red. Refluxing the dark red solution leads to a 67.7% yield of red-black, highly insoluble material (94) which exists as hard microcrystals. The unknown material 94 has a melting point which varies from batch to batch.

The analytical and spectral data for 94 were of poor quality and uniformative. The elemental analysis for 94 did not indicate a 1:1 adduct; but, rather, it indicated that 94 was contaminated with a small amount of benzene. Despite the fact that 94 analyzed low for both nitrogen and chlorine (see Chapter V), it was assumed that 94 could be best described as a 1:1 adduct between DDQ and 6. A good, consistent mass spectrum could never be obtained for 94 and, even in trifluoroacetic acid (TFA), 94 was not soluble enough to produce a useful NMR spectrum. The IR spectrum of 94 indicated absorptions for C-H stretch, nitrile (singlet, 2200 cm^{-1}), and C=C stretch.

Since DDQ often contains traces of hydrogen chloride due to reaction with atmospheric water, it was hypothesized that perhaps 6 converted into the known 3,6-diphenyl-4-methylpyridazine (95)[3] by acid-catalyzed ring-opening.[3] The 95 thus formed might then complex with DDQ to form 94. However, 95 was found not to react with DDQ under the conditions used in the formation of 94.

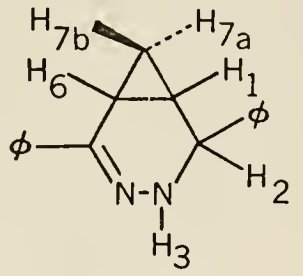
The reaction of 94 with sodium borohydride in acetonitrile produced a new, colorless compound 96 in 26.5% yield.

The mass spectrum of 96 displayed a parent ion at m/e 248 while an elemental analysis indicated that 96 was a dihydroderivative of 6. The IR spectrum of 96 indicated the presence of amine hydrogen and a carbon-nitrogen double bond.

In the aromatic region of the NMR spectrum, 96 displayed two multiplets centered at τ2.25 and 2.68 integrating for two and eight protons respectively. As in previous cases (vide supra), the two multiplets are assumed to account for the ortho protons of the phenyl attached to a carbon-nitrogen double bond and the remaining protons. The upfield portion of the NMR spectrum of 96 consisted of a very broad one-proton singlet at τ4.59, a broad one-proton singlet at 5.92, a three-proton multiplet centered at 7.95, and a one-proton multiplet centered at 8.95. On the basis of the above spectral data, 96 is thought to be the product of the sodium borohydride reduction of 6 which is somehow complexed with DDQ. The upfield portion of the NMR spectrum of 96 is assigned as shown in Table XI. The stereochemistry shown is assigned assuming attack on the carbon-nitrogen double bond from below the six-membered ring of the diazanorcaradiene 6. The reduction of one carbon-nitrogen double bond of 6 is not surprising in view of the results of Heinrichs and et.al.;[5] however, complex hydride reductions of diazanorcaradienes have not been reported previously.

Table XI

Proton Assignments for 96



96

Proton	Assignment
1	τ7.95 mult.
2	5.92 sing.
3	4.59 sing.
6	7.95 mult.
7a	7.95 mult.
7b	8.95 mult.

Confirming the above conclusions, it was found that 96 is formed quantitatively on reacting 6 with sodium borohydride in acetonitrile. Thus, it seems clear that the complex 94 contains 6 which has retained its original structural identity. If the material 95 was merely polymer or insoluble tar containing 26.5% 6, then 6 should have been easily leached out in TFA (vide supra) and displayed the characteristic NMR spectrum of 6 in TFA. Protonated 6 in TFA solution is stable at room temperature for several weeks. Since the reduction of 94 by borohydride produced only a 26.5% yield of 96 and the reduction of 6 by borohydride is quantitative, there is some question as to whether 94 can be described accurately as a 1:1 complex between DDQ and 6.

To date, the structure of 94, if it is a pure compound, is still unknown.

The reaction of trityl fluoroborate with 6 at room temperature did not proceed at any measurable rate. Heating a mixture of 6 and trityl fluoroborate in acetonitrile produced nothing but unidentified black tar.

Upon finding that 3 is a 4H-diazepine rather than a bicyclic compound[2] (see Chapter I), it was decided to attempt a synthesis of 3,4,5,6,7-pentaphenyl-1,2-diazatropylium bromide *via* a route similar to that used by Doering and Knox[65] in the synthesis of tropylium bromide.

Reaction of 3 with excess bromine in carbon tetrachloride produced a yellow, crystalline material (97) which was too unstable to obtain anything more than an NMR spectrum. The NMR spectrum of the yellow 97 consisted of a two-proton multiplet centered at τ2.27, a twenty-three-proton multiplet centered at 2.86, and a broad one-proton singlet at 3.95. The NMR spectrum of the precursor 3 shows, in addition to the aromatic multiplet, a broad singlet at τ4.10. On the basis of the previous work of Maier[16] and the NMR spectrum, the yellow 97 was tentatively identified as the N-bromobromide salt of 3.

No attempt was made to react 3 with trityl cation as, from previous studies,[69] the abstraction of a hydride from a carbon bonded to a phenyl ring is extremely difficult.

Facile access to large amounts of the recently synthesized 3,5,7-triphenyl-4H-1,2-diazepine (26)[17] gave strong impetus to an attempt at the synthesis of 3,5,7-triphenyl-1,2-diazatropylium salts. In view of the reaction of

bromine with 3, the method of Doering and Knox[65] was not considered. Rather, the synthetic method of Dauben[68] was deemed to have the greater possibility of success. Although the 1,3,5-triphenyltropylium cation has apparently never been synthesized, it was assumed that steric effects due to the 3- and 5-phenyls would not hinder abstraction of a hydride from 26. It should be noted that the 4-position of 26 has only hydrogen bonded to it.

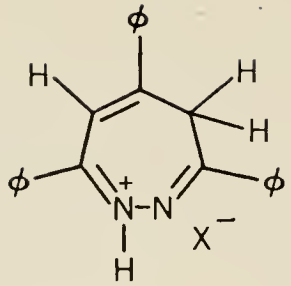
Reaction of 26 with trityl perchlorate at room temperature gave a 30.5% yield of a yellow, crystalline material (98) which analyzed correctly for the desired diazatropylium perchlorate salt. However, the NMR spectrum, which consisted of a sixteen-proton multiplet centered at τ2.27 and a broad two-proton singlet at 5.70, indicated that two non-aromatic protons were still present. The IR spectrum of 98 indicated the presence of hydrogen attached to nitrogen (3100 cm^{-1}) and fluoroborate anion (1100 to 1040 cm^{-1}).

Fluoroborate salts are known for their volatility and ability to be vaporized for mass spectral analysis.[70] The fluoroborate salt 99 was no exception. The mass spectrum of 99 was found to be very similar to the reported[17] mass spectrum for the precursor 26 which is not what would have been expected had 99 been triphenyldiazatropylium fluoroborate. A parent ion at m/e 221 rather than the parent ion found at m/e 222 would have been expected if 99 was the desired diazatropylium.

If the trityl cation had extracted a hydride ion from 26 in forming 99, triphenylmethane should have been present in the reaction mixture.[68] Chromatography of the complex, highly colored mother liquor from the above reaction yielded no triphenylmethane.

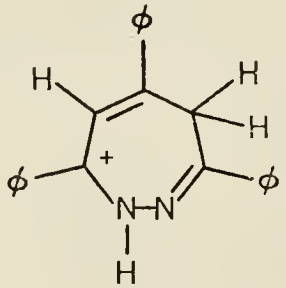
On mixing a small quantity of 99 with sodium borohydride in acetonitrile, gas evolved and 26 was regenerated. Presumably the gas was hydrogen produced by the reaction of sodium borohydride with a protonated amine. The diazepine 26 should be regenerated on reaction of the diazatropylium cation with sodium borohydride but the reaction should proceed without the evolution of hydrogen.

The above results lead to the conclusion that the yellow salts isolated in the above reactions were 3,5,7-triphenyl-4H-1,2-diazepine hydroperchlorate (98) and 3,5,7-triphenyl-4H-1,2-diazepine hydrofluoroborate (99). As a final check on this structural assignment it was found that reaction of 26 with perchloric acid in acetic anhydride produced 98 identical in all respects to the 98 produced above. Perchlorate 98 and fluoroborate 99 are assumed to be formed by reaction of 26 with the corresponding acid which results from reaction of the trityl cation with moisture which inadvertantly enters the reaction vessel.



98 X = ClO_4^-
99 X = BF_4^-

The NMR spectrum of 98 and 99 is in good agreement with the structure assigned. The 6-proton whose NMR absorbance is at τ3.32 in 26 is now shifted into the aromatic multiplet by resonance structures such as 100 and the inductive effect of the positive charge on nitrogen. The two

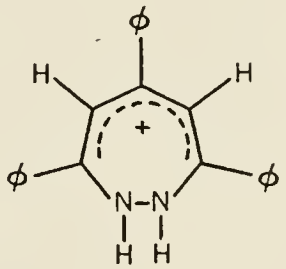


100

protons at C-4, which appear as a doublet of doublets in the neutral 26 due to the rigidity of the diazepine ring,[17] now absorb as a very broad singlet at ambient temperatures since, for unknown reasons, the diazepine ring is now free to rapidly ring invert and thus interchange the chemical shifts of the two protons in the 4-position.

At present, it is not known which nitrogen the acidic proton is bonded to in 98 and 99. The proton attached to nitrogen is assumed to be exchanging at such a rate that it cannot be detected by NMR methods.

At the same time 98 and 99 were discovered and characterized, similar reactions were carried out by Carty.[71] Carty, however, assigned 98 and 99 the structure 101, which is a cyclic eight π-electron antiaromatic system.



101

Carty[71] claimed that the τ5.70 signal in the NMR spectrum was due to two equivalent N-H protons whose signal was somewhat broadened due to the quadrupole moment of nitrogen and chemical exchange. The other data obtained in this work such as the mass spectrum of 99 and the reaction of 99 with sodium borohydride were explained by a rapid, allowed 1,5-hydrogen shift from N-1 to C-4.

If structure 101 was the true structure for 98 and 99, lowering the temperature of a solution of either 98 or 99 should cause no change in the NMR spectrum of either of these compounds. On the other hand, if the structures assigned in this work are correct, the signal at τ5.70 should broaden further, disappear, and transform into a

Figure 24. NMR spectrum of 3,5,7-triphenyl-4H-1,2-diazepine hydrofluoroborate (99) in TFA/$CDCl_3$ at 17.0°

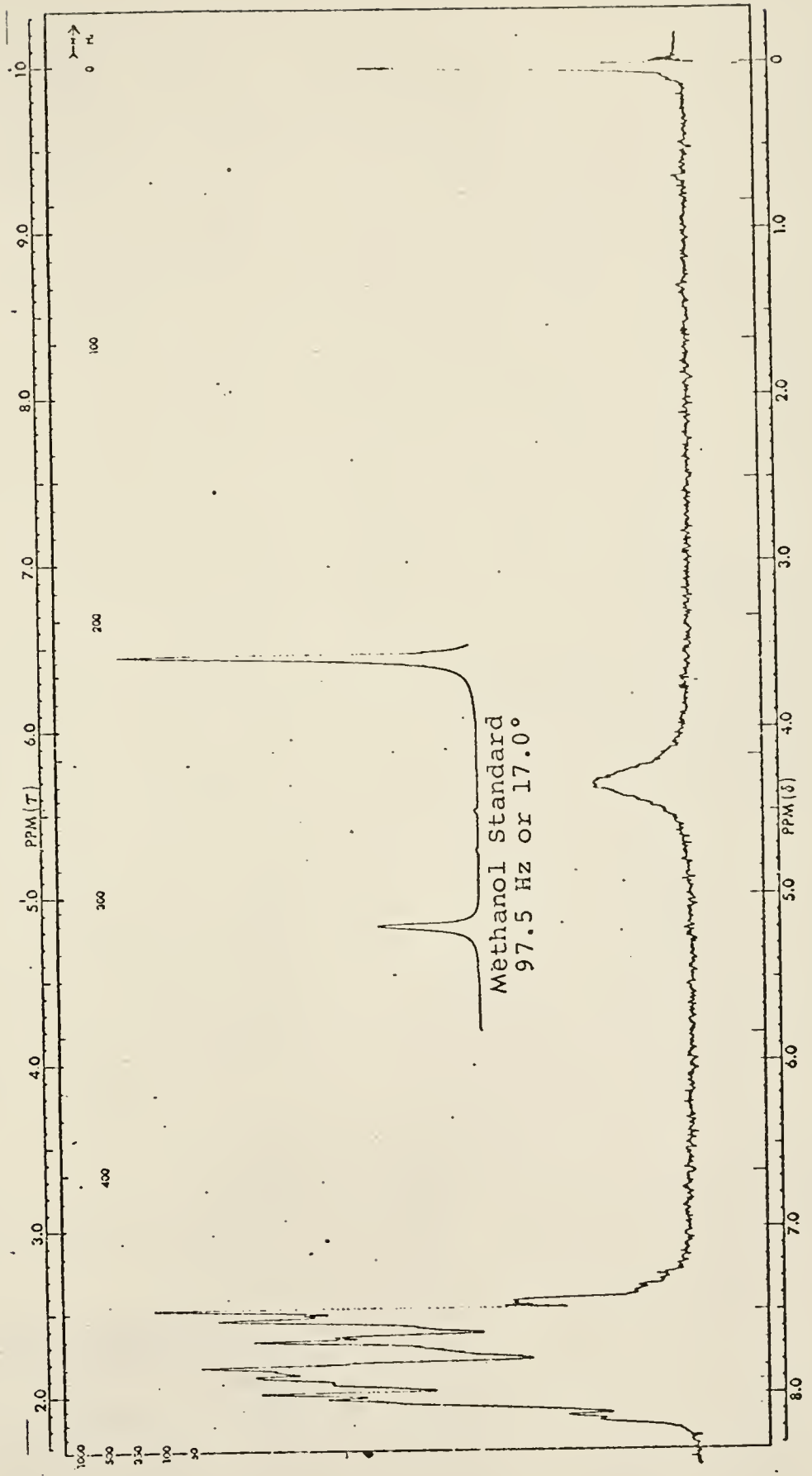

Methanol Standard
97.5 Hz or 17.0°
PPM(τ)
PPM(δ)
Hz

Figure 25. NMR spectrum of 3,5,7-triphenyl-4H-1,2-diazepine hydrofluoroborate (99) in TFA/$CDCl_3$ at 1.5°

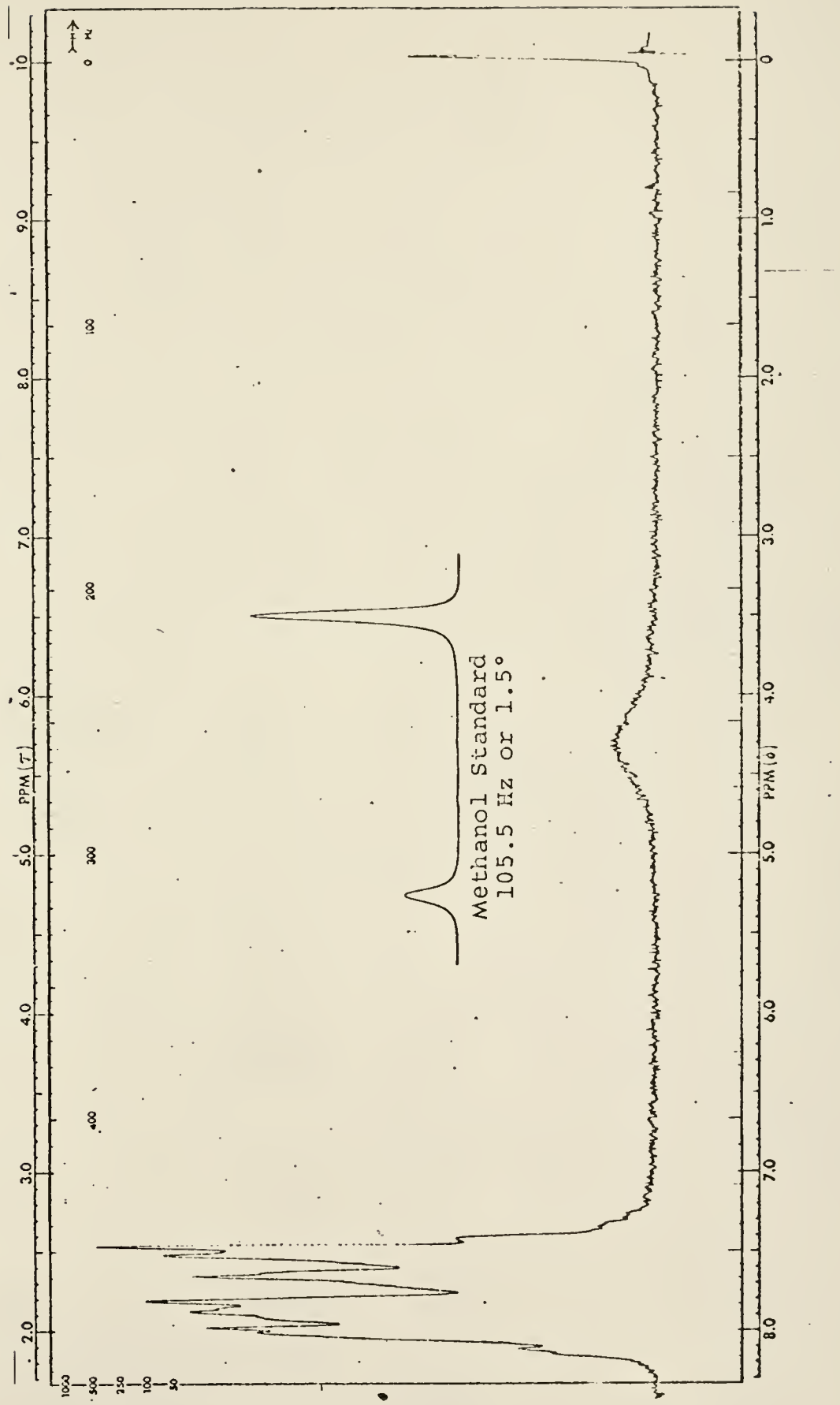
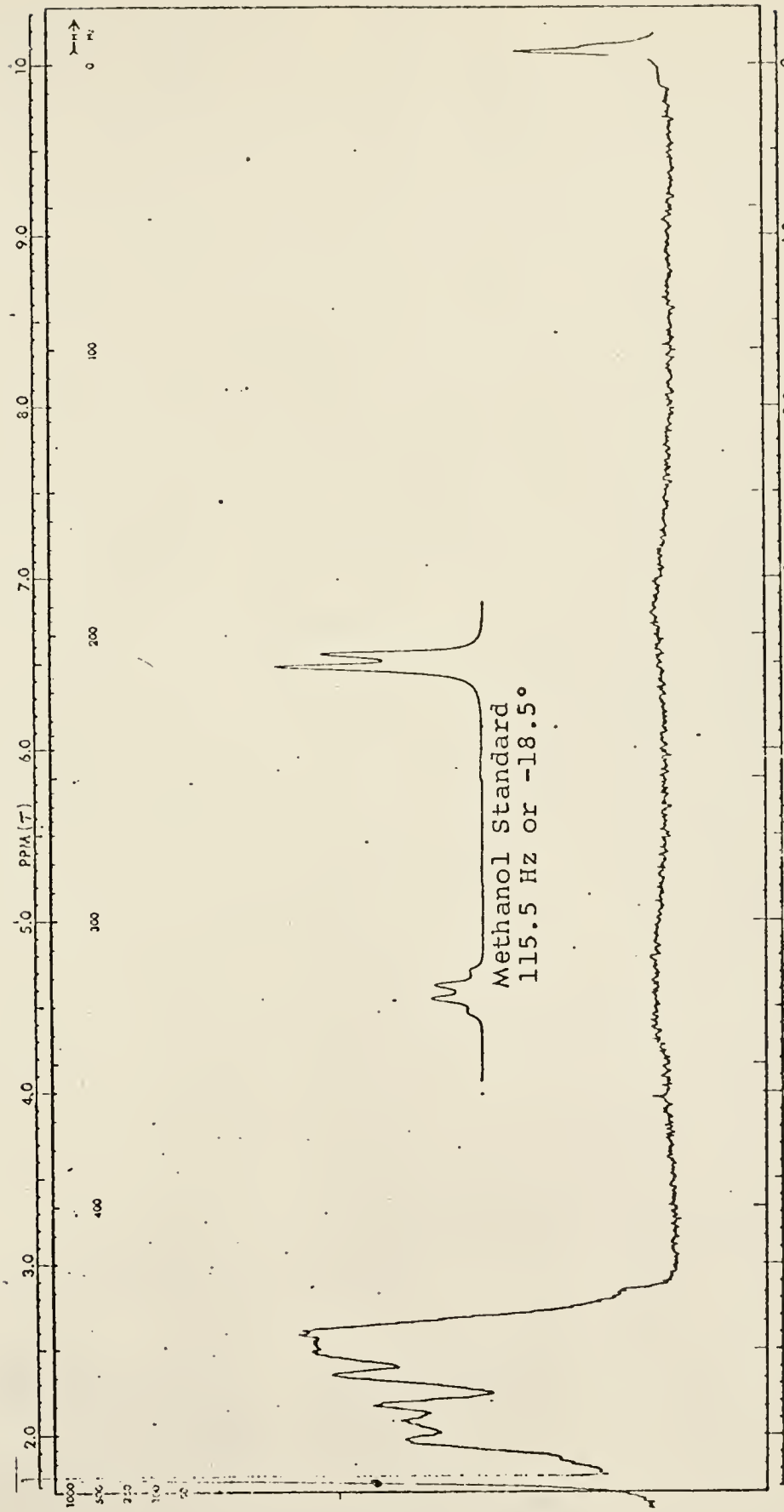

Methanol Standard
105.5 Hz or 1.5°
PPM(τ)
PPM(δ)
0 Hz
100
200
300
400
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
1000
500
250
100
50

Figure 26. NMR spectrum of 3,5,7-tripheny1-4H-1,2-diazepine hydrofluoroborate (99) in TFA/$CDCl_3$ at -18.5°


Methanol Standard
115.5 Hz or -18.5°
PPM(τ)
PPM(δ)

doublet of doublets symmetrically displaced about the original 5.70 signal.

As illustrated in Figures 24 through 26, the τ5.70 singlet does collapse and two new signals symmetrically displaced about the original signal appear at about 4.6 and 6.8. Due to crystallization of 99 from the TFA solution at low temperatures, an NMR spectrum of 99 in a frozen conformation could not be obtained. However, the data obtained do indicate that the structures as assigned in this work are correct.

In a final attempt at the synthesis of the 3,5,7-triphenyl-1,2-diazatropylium cation equimolar quantities of 26 and DDQ were mixed in benzene at room temperature to give a very deep red solution. After stirring for about an hour, the red solution began to deposit colorless needles. As crystallization proceeded, the red color of the solution faded. An 88.5% total yield of colorless crystals of unknown 102 was isolated. The colorless crystals tended to yellow very slightly on isolation.

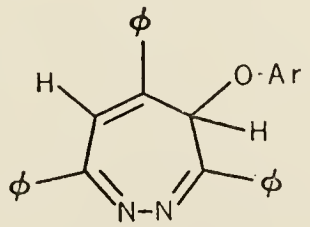
Elemental analysis and mass spectrometric measurement indicated that 102 was a 1:1 complex between 26 and DDQ.

The NMR spectrum of 102 was very uninformative as it displayed only a multiplet at τ1.6 - 2.7. Any tropylium-type protons would have been expected to absorb at around τ0.5[72] in the absence of any shielding effects from the phenyl rings bonded to the diazepine ring. The IR spectrum

of 102 indicated nitrile (singlet 2200 cm^{-1}) and C=C stretch. Moisture in the potassium bromide mulling agent prevented the detection of any O-H stretch.

The UV spectrum of 102 (Figure 27) is essentially the UV spectrum of 26[17] with the exception of the new band at 221 nm and the intensities of the main absorption maxima.

On the basis of the above information, 102 was tentatively assigned the diazepine structure given below. The NMR spectrum is explained by assuming that protons at C-4 and C-6 are inductively shifted downfield into the aromatic region of the spectrum due to both the strongly electron-withdrawing hydroxydichlorodicyanophenylether group at C-4 and the presumed dipolar character of the diazepine-oxygen bond at C-4. The UV spectrum is consistent with 102's similarity to the precursor 26 and the presence of the hydroxydichlorodicyanophenyl ether function at C-4 which may be the cause of the new band at 221 nm. The insolubility of 102 is not unexpected.

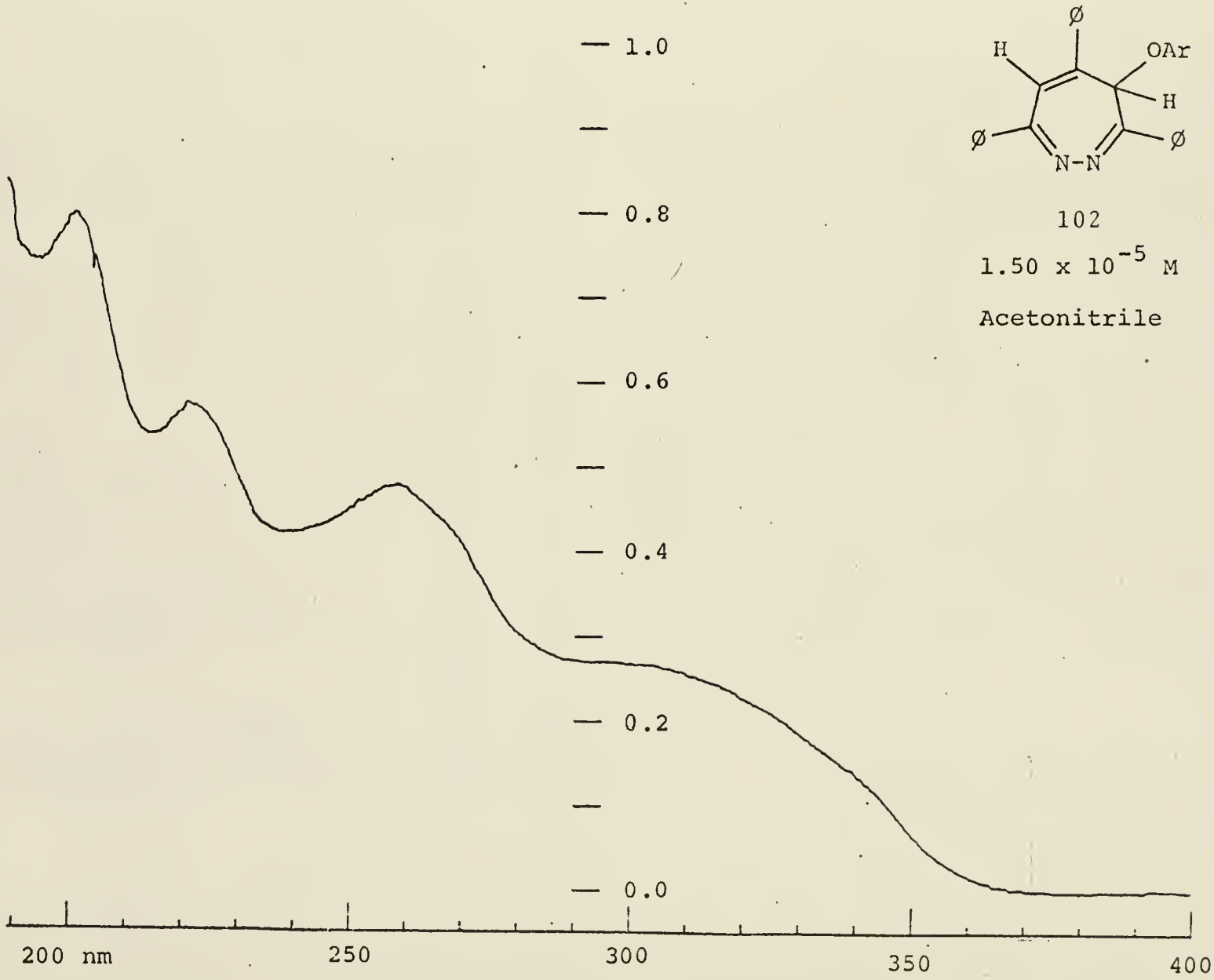


Ar = 4-hydroxy-2,3-dichloro-4,5-dicyanophenyl

102

From the above studies it would appear that the hypothetical 1,2-diazatropylium cation is either too

Figure 27. UV spectrum of unknown 102



102

1.50×10^{-5} M

Acetonitrile

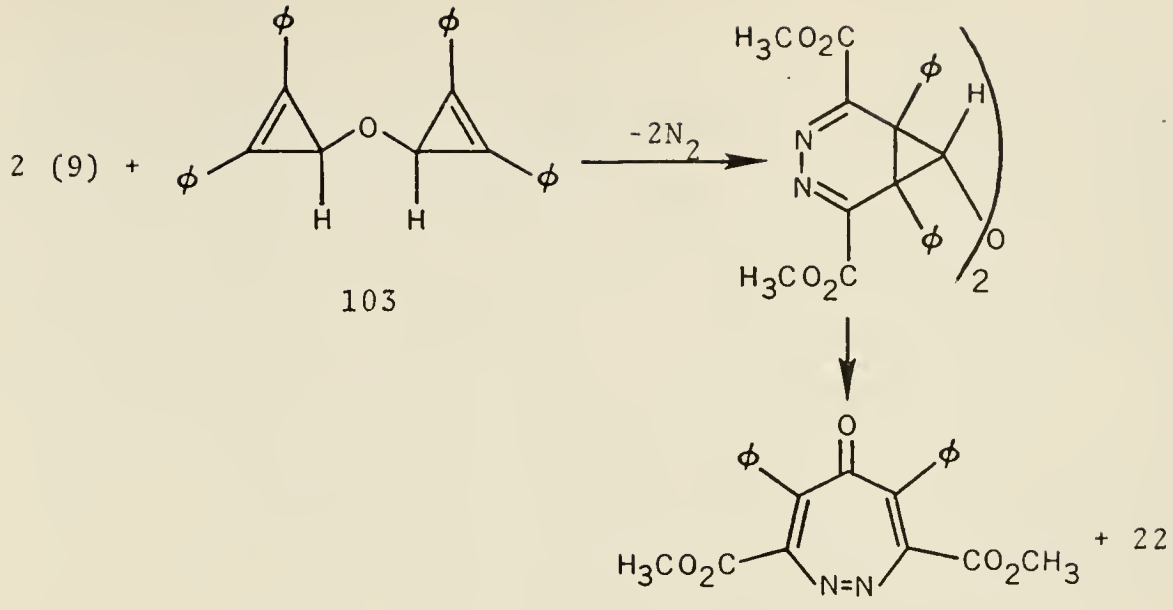
unstable to be synthesized or so unstable that synthesis will be difficult and must be approached by methods other than those employed in this work.

Attempted Syntheses of 1,2-Diazatropone

Among the many known synthetic routes to the carbocyclic tropone,[7] only two were followed in the attempted synthesis of 1,2-diazatropone. The first method, that of Radlick,[73] involved simple oxidation of cycloheptatriene directly to tropone using selenium dioxide. The second method was designed after the report of Harmon et al.[74] that pyrolysis of ditropenyl ether in the presence of moist alumina and phosphorus pentoxide yielded, by disproportionation, tropone and cycloheptatriene. Other synthetic routes which lacked literature precedence were also probed.

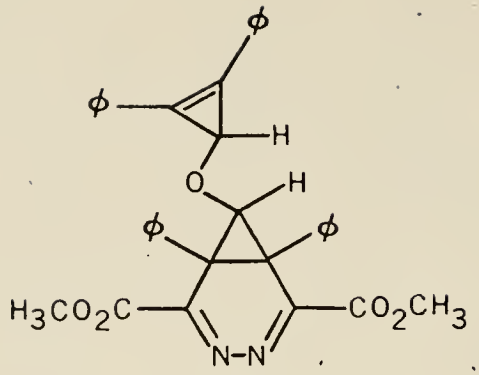
Assuming that it would have the best chance of undergoing oxidation, diazanorcaradiene 22 was treated with selenium dioxide according to Radlick's[73] procedure. No identifiable product resulted from the attempted oxidation. No attempt was made at oxidizing the 4H-diazepine 26.

In adapting Harmon's[74] synthesis of tropone to a 1,2-diaza system the reaction sequence of Scheme 25 was employed. It was assumed the 22 and the 1,2-diazatropone could be separated by chromatography.



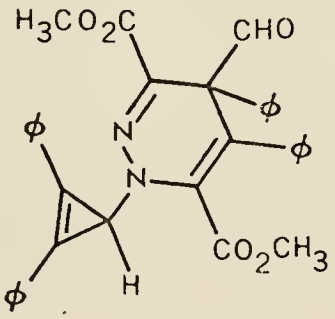
Scheme 25

Reaction of two moles of tetrazine 9 with one mole of ether 103 yielded a mixture of product and unreacted tetrazine which could not be separated easily. Repeating the reaction using a 1:1 molar ratio of reactants yielded a bright yellow crystalline compound 104 which gave a mass spectral molecular weight of 568 and an elemental analysis consistent with a 1:1 adduct. The UV spectrum of 104 (Figure 28) indicated that a diphenylcyclopropenyl moiety attached to an electron-withdrawing element or group was still present. The above data were consistent with assigning the new compound the diazanorcaradiene structure 105.



105

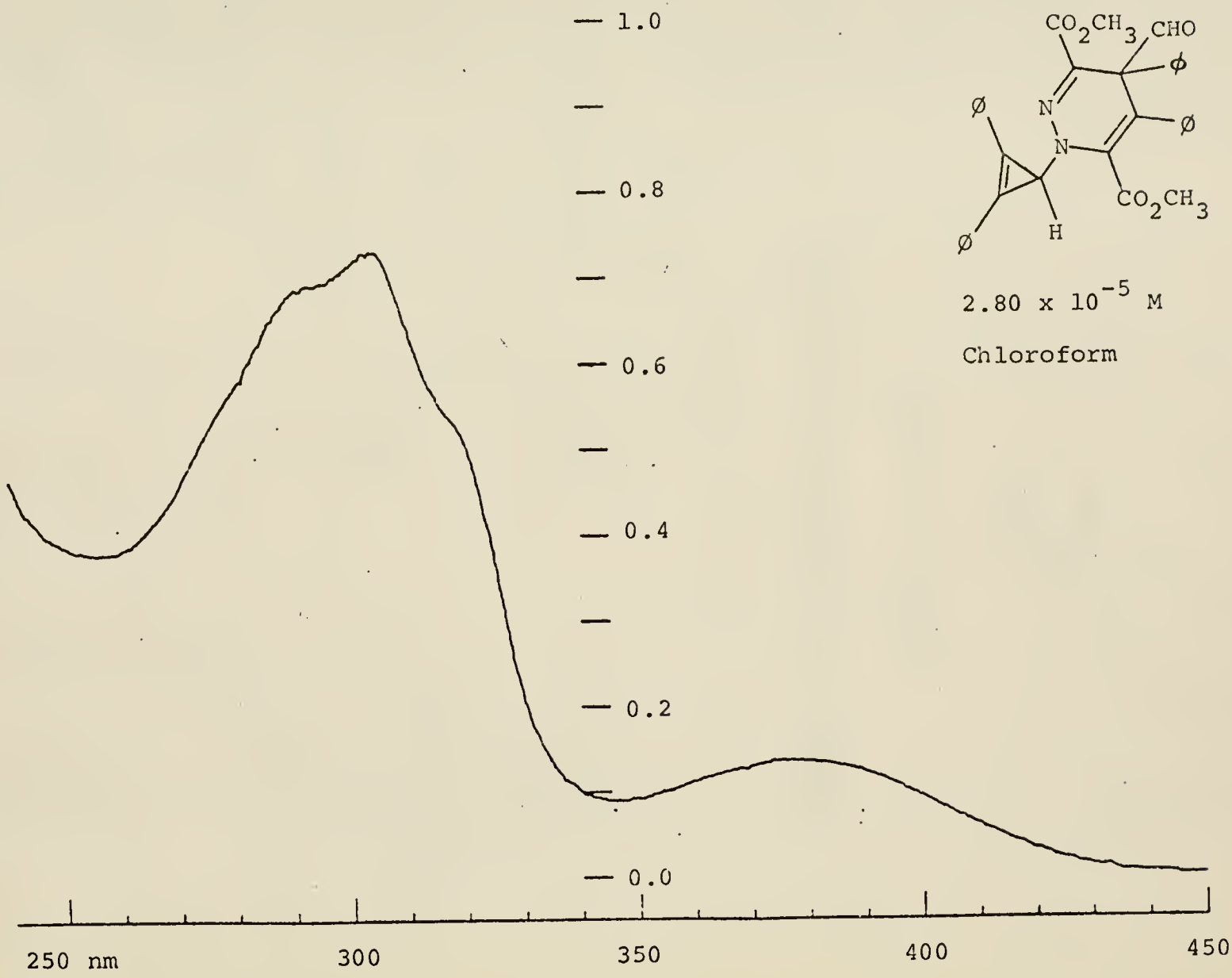
However, both the NMR and IR spectra indicated that the ester groups of 104 were nonequivalent which is not in accord with the symmetrical structure 105. Other features of the NMR spectrum indicated that 104 should be assigned the structure given below.



104

The NMR spectrum of 104 showed the aldehyde protons as a sharp one-proton singlet at τ1.08, the phenyl protons as a multiplet in the 1.93 to 3.23 region, and the cyclopropene proton as a sharp one-proton singlet at 5.32. The non-equivalent ester methyls manifest themselves by two sharp three-proton singlets at τ6.42 and 6.52.

Figure 28. UV spectrum of 4,5-diphenyl-3,6-dicarbomethoxy-1-(1,2-diphenylcyclopropen-3-yl)-1,4-dihydropyridazine-4-aldehyde (104)


1.0
0.8
0.6
0.4
0.2
0.0
250 nm
300
350
400
450
CO2CH3
CHO
ϕ
Ø
N
N
Ø
CO2CH3
Ø
H
2.80 x 10-5 M
Chloroform

As expected, the mass spectrum of 104 shows no measurable peaks for loss of either benzonitrile or methyl cyanoformate (see Chapter II). Also, as anticipated, the base peak is at m/e 191 which can be accounted for by diphenylcyclopropenyl cation formation. There is no peak for diphenylcyclopropenone.

Diesteraldehyde 104 is simply a member of the well-known dihydropyridazines[1] which are yellow when the 3- and 6-positions are substituted with ester groups. The visible spectrum of 104 displays the expected weak $n \rightarrow \pi^*$ band at 590 nm ($\varepsilon = \sim 180$) while the UV spectrum (Figure 28) is consistent with a diphenyl-cyclopropenyl group attached to an electron-withdrawing element or group.[75]

Although only two carbonyl stretches could be identified in the IR spectrum of 104, it is obvious from the NMR spectrum that the methyl ester functions are nonequivalent. The characteristic aldehydic carbon-hydrogen stretches[76] were located as two weak bands at 2840 and 2730 cm^{-1}.

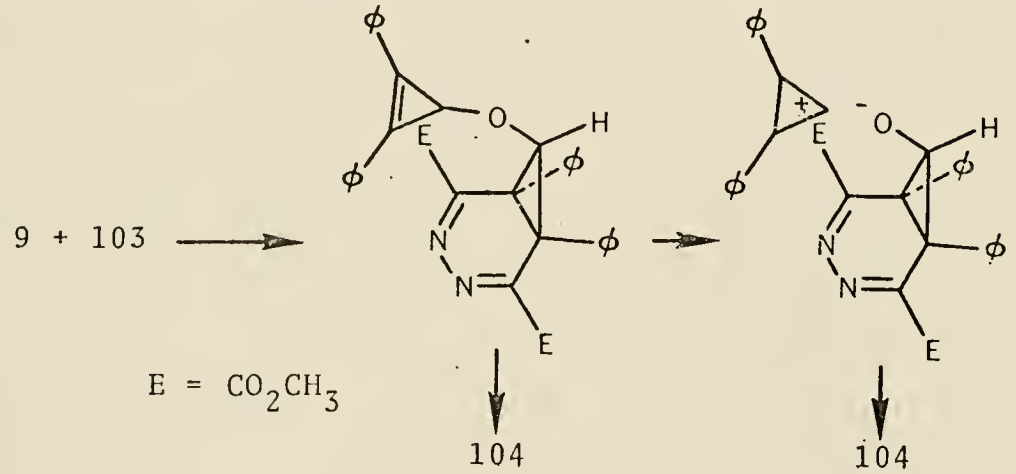
That 104 fails to add another mole of the powerful diene 9 at room temperature is in complete accord with previous observations.[2] Diphenylcyclopropenes with powerful electron-withdrawing substituents in the 3-position invariably exhibit low dieneophilicity. No attempt was made at reacting 9 with a second mole of tetrazine under forcing conditions.

Unfortunately, an attempt at completely oxidizing 104 to the fully aromatic, easily synthesized dimethyl

4,5-diphenylpyridazine-3,6-dicarboxylate was an apparent failure.

Although the reaction between 9 and 103 did not produce the desired bisdiazanorcaradienyl ether or even the equally desirable diazanorcaradienyldiphenylcyclopropenyl ether 105, the formation of 104 is of extreme interest.

Mechanistically, the monoadduct 105 is almost certainly the initial product, but rearrangement by either of the paths shown in Scheme 26 leads to 104. It should be stressed at this point that 104 was formed at room temperature and no heat was ever applied to the reaction mixture.



Scheme 26

No evidence for either mechanism exists at the present time. The similarity between the concerted, allowed $(\pi 2s + \pi 2s + \sigma 2s)^{12}$ mechanism (path a above) and the Cope-type mechanism proposed in Chapter I should be noted especially in view of the results of the x-ray study on the diazanorcaradiene (66)-diazepine (67) system. It should be pointed out that the ionic mechanism (path b above) is also

quite reasonable in view of the known stability of the diphenylcyclopropenium cation.[75] Another mechanism for the conversion of 105 into 104 involves a concerted, allowed [1,5] shift of the diphenylcyclopropenyl group of 105 from oxygen to nitrogen.

Since the difficulty encountered in attempting to utilize Scheme 25 could not be bypassed, other synthetic schemes were considered.

Although diphenylcyclopropenone[77] is known to have aromatic properties, the possibility that it might undergo the Diels-Alder reaction with the powerful diene 9 was considered. Unfortunately, as was anticipated, the attempted reaction of 9 and diphenylcyclopropenone produced a complex mixture which seemed to consist mostly of unreacted, impure diphenylcyclopropenone.

In order to bypass the stability of diphenylcyclopropenone, the aromatic diphenylcyclopropenone was converted into the known diphenylcyclopropenone ethylene ketal 106.[78] Reaction between 9 and 106 was sluggish as expected (vide supra - 104), and the reaction mixture was again a complex mixture which defied identification even after chromatography over basic alumina.

Unfortunately, the synthetic schemes utilized in this work in the attempted production of 1,2-diazatropone have either failed at such early stages or for such theoretically sound reasons that nothing concrete can be said about the stability or ease of production of 1,2-diazatropone.

However, in view of the results in the diazatropylium series, it is felt that diazatropone will also be a relatively inaccessible system.

CHAPTER V

EXPERIMENTAL

General

All melting points were obtained using either a Thomas-Hoover or Mel-temp melting point apparatus and are uncorrected. Analytical gas-liquid chromatographic (glpc) work was done on an Aerograph Hy-Fi Model 600-D equipped with a hydrogen flame ionization detector. Preparative glpc work was performed on an Aerograph A-90-P instrument. Elemental analyses were obtained from Galbraith Laboratories, Peninsular ChemResearch, or Atlantic Microlabs.

Spectra

Mass spectra were obtained on a Perkin-Hitachi RMU-6E mass spectrometer at 70 ev. Mass spectra are listed by mass (m/e) unit with the relative intensity in parentheses next to the mass unit. Unless the mass spectral peak has some special significance or analytical value, only those peaks of 10% or greater relative intensity are listed. Where it was necessary to give a plot of the whole spectrum, the plots are given as figures as indicated.

Nuclear magnetic resonance (NMR) spectra, unless stated otherwise, were recorded on either a Varian A-60 or A-60A instrument. All standard symbols and abbreviations are used.

Ultraviolet (UV) and visible spectra were obtained using a Cary Model 15 recording spectrophotometer. UV and visible absorbances are listed by wavelength (nm) with the molar extinction coefficient in parentheses next to the wavelength. Standard abbreviations are used. No molar extinction coefficient is assigned to inflections.

Infrared (IR) spectra were procured on either a Perkin-Elmer Model 137 or Model 337 and selected absorbances are listed by wavenumber (cm^{-1}).

Temperature-Dependent NMR Spectra

All temperature-dependent NMR spectra were recorded on a Varian A-60A instrument. Except as noted, temperatures greater than 40° were accurately determined by the chemical shift difference between the hydroxyl and methylene hydrogens of ethylene glycol. Except as noted, temperatures lower than 40° were accurately determined from the chemical shift differance between the hydroxyl and methyl hydrogens of methanol.

3,6-Bis(4-iodophenyl)-1,2,4,5-tetrazine (17)

Using the method of Abdel-Rahman *et al.*[10] 20.9 g (91.2 mmoles) of freshly chromatographed (basic alumina) *p*-iodobenzonitrile, 18.2 g (364 mmoles) of hydrazine hydrate, 1.67 g (52.1 mmoles) of flowers of sulfur, and 150 ml of absolute ethanol were combined to form a dark red mixture which was refluxed for 2 hours to yield an almost completely solid, orange mixture. Filtration gave 16.0 g (32.8 mmoles

or 71.9%) of yellow 1,2-dihydro-3,6-bis(4-iodophenyl)-1,2,4,5-tetrazine.

To 2.0 g (4.1 mmoles) of the dihydrotetrazine dissolved in 150 ml of acetone was added excess anhydrous iron trichloride powder. The resulting purple sludge was filtered, washed with water and dimethyl formamide, and recrystallized from xylene to give 0.90 g (1.9 mmoles or 45%) of 17 as purple leaflets, mp 308-310° (dec.). Final purification to remove small amounts of what was later tentatively identified as 2,5-bis(4-iodophenyl)-1,3,4-thiadiazole (18) was accomplished by rapidly passing the compound in boiling xylene over basic alumina. If the tetrazine remained in contact with the alumina too long, the characteristic purple color of the tetrazine was destroyed indicating total decompostion. The IR of this tetrazine was very similar to that for the known 3,6-bis(4-bromophenyl)-1,2,4,5-tetrazine (65).[6]

Mass Spectrum: 487 (1.5%), 486 (8%), 229 (100%), 101 (95%), 75 (23%), 51 (18%).

Infrared (KBr): 2920, 1580, 1495, 1320, 1185, 1057, 1003, 919, 840, 825, 727, 710, 590 cm^{-1}.

3,7-Bis(4-iodophenyl)-4,5,6-triphenyl-4H-1,2-diazepine (19)

A solution of 2.03 g (4.18 mmoles) of unchromatographed 17 in 200 ml of xylene containing 1.23 g (4.59 mmoles) of sym-triphenylcyclopropene[29] was refluxed 22 hours with additional small amounts of the cyclopropene added near the end to completely remove the red coloration.

The xylene was flash evaporated and the almost colorless

residue dissolved in chloroform and filtered. Crystals were obtained on addition of low-boiling petroleum ether to the chloroform solution. Final purification was accomplished by chromatography over silica gel which gave 1.22 g (1.68 mmoles or 40.3%) of very pale green crystals of 19, mp 249.0-249.5°.

Mass Spectrum: 728 (2%), 727 (8%), 726 (21%), 699 (15%), 698 (38%), 623 (39%), 498 (32%), 497 (100%), 496 (24%), 269 (17%), 268 (19%), 266 (20%), 230 (13%), 150 (50%), 103 (15%), 87 (23%), 86 (36%), 85 (37%), 84 (59%), 60 (15%), 45 (18%).

Analysis for $C_{35}H_{24}I_2N_2$:

element	calculated	found
C	57.87%	57.73%
H	3.32%	3.48%

NMR ($CDCl_3$):

τ2.25-3.04	multiplet	26H
4.17	br. singlet	1H

Infrared (KBr): 2940, 1595, 1460, 1010, 1000, 828, 770, 745, 713, 700 cm^{-1}.

Kinetics of the Thermal Rearrangement of 1,2,5,6,7-Pentaphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (2) to 3,4,5,6,7-Pentaphenyl-4H-1,2-diazepine (3).

Kinetic runs were made at 150.0°C and 140.0°C by following the disappearance of the cyclopropyl absorbance of 2 in the NMR with fluorene as an internal standard.

Kinetic solutions were made up of about 40 mg of 2 and

10 mg of fluorene both accurately weighed and dissolved in the standard amount of d_5-nitrobenzene in an NMR tube which was then sealed with a pressure cap.

Kinetic values for 2 relative to the internal standard were taken from at least three good integrals. Integrals which were exceptionally noisy were discarded. The kinetic parameters were obtained from a least squares plot.

2,5,7-Triphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (7)

The stirring of 1.27 g (3.90 mmoles) of trans-1,2-dibenzoyl-3-phenylcyclopropane (31), 90 mg of sodium hydroxide, and 0.50 ml (10 mmoles) of hydrazine hydrate in 500 ml of absolute ethanol for 72 hours resulted in formation of a yellow suspended solid. Filtration followed by recrystallization from 95% ethanol yielded two crops of bright yellow needles weighing 629 mg and 58.1 mg (total: 2.15 mmoles or 55.1%; lit.[4]: 16%) and melting, respectively, at 232-233° and 228.5-230° with decomposition (lit.[4] mp 235°). Spectra were in agreement with those reported.[4]

Thermal Rearrangement of (7)

A 103 mg sample of 7 was refluxed in 7 ml of dioxane for a total of 132 hours to yield a brown oil which showed no recognizable absorbances in the NMR. Chromatography over deactivated alumina gave two yellow bands, the NMR spectra of which also showed nothing recognizable.

Check on the Thermal Stability of the Anticipated Thermal Rearrangement Product of 7

A 115 mg sample of 3,5,7-triphenyl-4H-1,2-diazepine (26) was refluxed for 132 hours in dioxane and the residue resulting from removal of solvent was recrystallized from ethanol to yield 73.2 mg (63.7% recovery) of starting material, mp 189-191°. Another recrystallization raised the melting point to 191.8-192.5°. The recovered material had an NMR spectrum identical to that of authentic 26.

Attempted Thermal Rearrangement of 2,5-Diphenyl-3,4-diaza-bicyclo[4.1.0]hepta-2,4-diene (6)[2]

A 93.4 mg sample of 6[2] was refluxed in xylene containing a few drops of N,N-dimethylaniline as a proton scavenger for 18 hours to yield, after chromatography over silica gel, only a small amount of tar and an undetermined amount of starting material. The recovered material gave the same NMR spectrum as authentic 6.

1,2-Diphenylcyclopropene[13]

1,2-Diphenylcyclopropene was prepared by the method of Longone[13] in the reported yield but the product could never be obtained in completely crystalline form. Spectral properties agreed with those given by Longone.

Dimethyl 1,6-Diphenyl-3,4-diazabicyclo[4.1.0]-hepta-2,4-diene-2,5-dicarboxylate (22)

To 619 mg (95% purity assumed from NMR, 3.06 mmoles) of

1,2-diphenylcyclopropene in 10 ml methylene chloride was added slowly a solution of 606 mg (3.06 mmoles) of dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (9) in 50 ml of methylene chloride until a very faint pinkness persisted. Flash evaporation of the methylene chloride from the now golden solution and washing with low-boiling petroleum ether yielded 984 (2.72 mmoles or 90% based on unused tetrazine) of yellow crystals of 22, mp 192.3-193.0° (dec.). Mixing diphenylcyclopropene with excess 9 invariably produced an intractable crystalline mixture.

Low temperature NMR work was done for this compound.

Mass Spectrum: 364 (5%), 363 (24%), 362 (100%), 329 (19%), 277 (35%), 259 (20%), 245 (33%), 212 (31%), 211 (34%), 210 (37%), 115 (13%).

Analysis for $C_{21}H_{18}N_2O_4$:

element	calculated	found
C	69.60%	69.70%
H	5.01%	5.18%
N	7.73%	7.87%

NMR ($CDCl_3$, -3.5°C):

τ2.95	singlet	10H	
6.35	singlet	6H	
6.37	doublet	1H	J=5.6 Hz
9.0	doublet	1H	J=5.6 Hz

Infrared (KBr): 2950, 1750, 1540, 1470, 1430, 1330, 1300, 1210, 1180, 1100, 830, 790, 775, 700 cm^{-1}.

Attempted Thermal Rearrangement of (22)

A 150 mg sample of 22 was refluxed in 10 ml of dioxane for 12 hours to yield a brown mixture which, on crystallization from chloroform-light petroleum ether or diethyl ether, gave a small amount of faintly colored needles, mp 123-123.5°. This compound is tentatively identified as dimethyl 1,6-diphenyl-3,4-diazabicyclo[4.1.0]hept-2-en-4-ol-2,5-dicarboxylate (26).

Mass Spectrum: 381 (8%), 380 (21%), 275 (15%), 261 (17%), 260 (64%), 229 (23%), 197 (32%), 192 (16%), 191 (12%), 190 (58%), 188 (20%), 157 (15%), 135 (36%), 134 (18%), 132 (15%), 120 (24%), 105 (100%), 78 (13%), 77 (60%), 52 (15%).

Analysis for $C_{21}H_{20}N_2O_5$:

element	calculated	found
C	66.30%	66.43%
H	5.30%	5.34%
N	7.37%	7.29%

NMR ($CDCl_3$):

τ1.15	br. singlet	1H	
2.75-3.18	multiplet	8H	
3.5-3.7	multiplet	2H	
4.75	br. singlet	1H	
6.18	sh. singlet	3H	
5.58	sh. singlet	3H	
6.78	AB quartet	2H	J_{AB}=12.5 Hz

Infrared (KBr): 3350, 3200, 3000, 2900, 1725, 1720, 1500, 1440, 1320, 1300, 1220, 767, 700 cm^{-1}.

Dimethyl 1,6-Diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5-dicarboxylate Hydrate (26)

A suspension of 74 mg of 22 in 10 ml of 4:1 water-dioxane was refluxed for 10 minutes to produce a colorless solution which was then extracted with chloroform. On concentration the chloroform solution yielded colorless, gummy crystals which, after washing with carbon tetrachloride and recrystallization from chloroform-light petroleum ether, melted at 127.7-128.0°. This compound gave an infrared similar to, but different from, that for the previously isolated 26.

1,2,5,6-Tetraphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (21)

A chloroform solution of 1,2-diphenylcyclopropene (339 mg, 94% purity assumed from NMR; 1.66 mmoles) and 3,6-diphenyl-1,2,4,5-tetrazine (1) (412 mg; 1.76 mmoles) was stirred for eleven days at room temperature. The solvent was flash evaporated from the still red solution and the residue chromatographed over basic alumina to yield 120 mg (0.513 mmoles) recovered tetrazine and 586 mg (1.47 mmoles) or 99.5% based on recovered tetrazine) bright yellow needles of 21, mp 207.5-208.0° (dec.).

High temperature NMR work was done on this compound. The temperatures were not accurately determined.

Mass Spectrum: 401 (2%), 400 (8%), 399 (11%), 398 (26%), 397 (8%), 371 (16%), 370 (37%), 296 (32%), 295 (100%), 294 (28%), 293 (16%), 192 (21%), 190 (30%), 189 (17%), 149 (24%), 103 (36%), 78 (34%).

Analysis for $C_{29}H_{22}N_2$:

element	calculated	found
C	87.40%	87.25%
H	5.57%	5.69%

NMR ($CDCl_3$):

τ2.0-2.36	multiplet	4H	
2.65-2.95	multiplet	6H	
3.16	singlet	10H	
6.31	doublet	1H	J=5.5 Hz
8.68	doublet	1H	J=5.5 Hz

Infrared (KBr): 2990, 1490, 1430, 1330, 1140, 1080, 1070, 1030, 1020, 930, 785, 715, 700, 695 cm^{-1}.

Attempted Preparation of 2,5,7,7-Tetraphenyl-3,4-diazabicyclo-[4.1.0]hepta-2,4-diene (29)

A solution of 7.508 g (18.68 mmoles) of trans-1,2-dibenzoyl-3,3-diphenylcyclopropane (32),[18] 1.84 ml (56.1 mmoles of anhydrous 97% hydrazine and 0.36 g (9.0 mmoles) of sodium hydroxide in 700 ml of absolute ethanol was refluxed for 72 hours during which time the mixture initially turned yellow but at the end was totally colorless. The solid which resulted on evaporation of solvent was recrystallized first from chloroform-hexane and then from 95% ethanol to yield two crops of colorless rhombs weighing a total of 4.85 g (12.2 mmoles or 65.6%). The first crop melted 185.7-186.0°. The compound was identified as 3,6-diphenyl-4-benzhydrylpyridazine (33).

Mass Spectrum: 400 (5%), 399 (29.9%), 398 (100%), 67 (13%), 65 (13%).

Analysis for $C_{29}H_{22}N_2$:

element	calculated	found
C	87.40%	87.39%
H	5.57%	5.61%
N	7.03%	6.98%

NMR ($CDCl_3$):

τ1.86-2.16	multiplet	2H
2.4-3.23	multiplet	19H
4.31	singlet	1H

Infrared (KBr): 2950, 1575, 1490, 1450, 1390, 1190, 1080, 1030, 1000, 790, 765, 740, 705, 700 cm^{-1}.

6,6-Diphenyl-2,4-diketo-3-oxabicyclo[3.1.0]hexane (34)

To a solution of 5.45 g (55.6 mmoles) of commercial maleic anhydride in 400 ml of warm benzene was added with magnetic stirring 11.99 g (61.75 mmoles) of diphenyldiazomethane[19] in a small amount of benzene. On mixing, immediate gas evolution and decolorization began. After stirring for 12 hours, the mixture was flash evaporated and the resulting slightly pink mass was broken up, washed with low-boiling petroleum ether, and recrystallized from cyclohexane to yield 9.0 g (34 mmoles or 61%; lit.,[20] 25.3%) snow-white, fine needles melting at 161.0-161.3° (lit.,[20] mp 162°). The NMR spectrum of 34 agreed with that given in the literature.[20]

3,3-Diphenyl-cis-1,2-cyclopropanedicarboxylic Acid (45)[18]

A mixture of 2.0 g (7.6 mmoles) of 34 and 0.8 g (20 mmoles) of sodium hydroxide in 100 ml of water was stirred at room temperature for 4 hours, filtered, and acidified to yield 1.9 g (6.7 mmoles or 89%) of crystalline 45, mp 201-202° (effervescence)-(lit.,[18] mp 204°). Recrystallization only served to lower the melting point.

Attempted Preparation of 7,7-Diphenyl-2,5-diketo-3,4-diaza-bicyclo[4.1.0]heptane (44)

A) A solution of 1.6 g (6.0 mmoles) of 45 in 600 ml of absolute ethanol was stirred for 4 days with 0.90 ml (0.87 g, 17 mmoles) of hydrazine hydrate. After flash evaporation of the ethanol, there remained a water-soluble substance which, on acidification, yielded 1.3 g (4.6 mmoles or 77% recovery) of starting material, mp 199.0-199.5°.

B) A mixture of 1.2 g (10.0 mmoles) of maleic hydrazide[25] and 2.04 g (10.5 mmoles) of diphenyldiazomethane[19] was stirred in 250 ml dimethyl formamide for 25 days after which period the solvent was flash evaporated to yield a gummy solid which produced nothing identifiable even after recrystallization from 95% ethanol.

C) A sample of 8.0 g (30 mmoles) of 34 was refluxed in 800 ml of absolute ethanol containing 2.25 ml (46 mmoles) of hydrazine hydrate for 60 hours. The ethanol was flash evaporated giving a crude solid which, on crystallization from a small amount of absolute ethanol, yielded 6.3 g

(23 mmoles or 75%) of colorless crystals of 44 (or its isomer - see Chapter I), mp 177.8-178.8°.

Mass Spectrum: 279 (2%), 278 (3%), 277 (1%), 262 (41%), 261 (41%), 233 (30%), 220 (39%), 219 (41%), 192 (64%), 191 (100%), 190 (14%), 189 (28%), 165 (38%), 115 (17%).

Analysis for $C_{17}H_{14}N_2O_2$:

element	calculated	found	
C	73.66%	73.66%	73.50%
H	5.07%	5.08%	5.17%
N	10.07%	10.04%	------

NMR ($CDCl_3$):

τ2.40-2.98	multiplet	10H
6.50	br. singlet	2H
6.88	singlet	2H

Infrared (KBr): 3350, 3290, 3050, 1730 1430, 1210, 1148, 910, 855, 775, 752, 704, 690, 545 cm^{-1}.

Attempted Preparation of 2,5,7,7-Tetraphenyl-3,4-diazabicyclo-[4.1.0]hepta-2,4-diene (29)

Assuming a 70% yield, 24.8 mmoles of phenyllithium were synthesized from 493 mg (71 mmoles) of lithium metal and 11.14 g (71 mmoles) of bromobenzene in 60 ml of dry diethyl ether.

The phenyllithium solution was added dropwise to a magnetically stirred solution of 1.40 g (5.02 mmoles) of 44 in 125 ml of dry benzene. A very dark, apparently yellow, reaction mixture was produced. The dark reaction mixture

was extracted with water, filtered, and dried to give an intractable yellow gum.

Attempted Preparation of exo-3,3-diphenyl-endo-2,4-dibenzoyl-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (39)

A mixture of 601 mg (2.00 mmoles) of 2,3-dibenzoylbicyclo-[2.2.1]hepta-2,5-diene (39)[22] and 408 mg (2.10 mmoles) of diphenyldiazomethane[19] was stirred for 24 days in 130 ml of benzene to produce a faintly yellow solution. Upon evaporation of solvent and exposure of the residue to the atmosphere, a deep purple petroleum ether insoluble substance appeared. On further exposure to the atmosphere, the purple residue transformed into a brown tarry mass.

Attempted Preparation of 7,7-Diphenyl-1,6-dibenzoylbicyclo-[4.1.0]hept-3-ene (42)

A solution of 993 mg (3.44 mmoles) of 1,2-dibenzoyl-cyclohexa-1,4-diene (41)[23] in 125 ml of benzene was combined with 700 mg (3.61 mmoles) of diphenyldiazomethane[19] with no apparent reaction. After one day of stirring at room temperature, there was still no perceptible reaction so the benzene was brought to reflux until all traces of diphenyl-diazomethane were gone. The NMR spectrum of this crude reaction mixture indicated much starting material, but no signals for the desired product. Additional diphenyl-diazomethane merely produced what was assumed to be benzo-phenone azine.

3,3-Diphenyl-2-cis-benzoylcyclopropanecarboxylic Acid (35)

A) Under anhydrous conditions, 9.75 g (73.1 mmoles) of aluminum chloride were added to 7.9 g (30 mmoles) of 34 in warm benzene with rapid mechanical stirring. The reaction was worked up by a procedure developed by Maier.[3] This involved adding the reaction mixture to aqueous hydrochloric acid, removing the benzene, filtration, dissolution of the filtrant in aqueous bicarbonate solution, filtration again, and precipitation of the ketoacid from the filtrate with mineral acid. The solid obtained in this case was a beige powder which consisted mostly of yellow, gummy resin.

Different experimental conditions were tried but none gave the desired compound.

B) Essentially the same reaction as in A) was run except that 1.601 g (6.061 mmoles) of 34 in 425 ml of dry benzene were added to 3.30 g (24.8 mmoles) of aluminum chloride in 200 ml of dry benzene over a 2-hour period with rapid mechanical stirring. Using Maier's workup after an additional 5.5 hours of stirring gave 1.61 g (4.71 mmoles or 77.7%) of a colorless compound, mp 217.8-218.8°, after recrystallization from chloroform-ligroin. The compound was tentatively identified as the trans isomer (37) of the desired compound.

Mass Spectrum: 343 (1.5%), 342 (3%), 297 (13%), 265 (20%), 264 (100%), 247 (11%), 221 (10%), 220 (53%), 219 (30%), 218 (13%), 192 (22%), 191 (20%), 189 (23%), 165 (13%), 105 (59%), 77 (12%).

Analysis for $C_{23}H_{18}O_3$:

element	calculated	found	
C	80.68%	77.50%	77.59%
H	5.30%	5.07%	5.07%

NMR ($CDCl_3$):

τ1.75-2.0	multiplet	
2.33-2.9	multiplet	
5.76	doublet	J≈6 Hz
6.37	doublet	J≈6 Hz

C) Using standard technique, 19.4 mmoles phenyl-magnesium bromide were prepared in 25 ml of dry diethyl ether.

The ether solution of the Grignard was added to 5.28 g (20.0 mmoles) of 34 over a period of 30 minutes. After stirring an additional 90 minutes the reaction mixture was poured onto 500 ml of ice-water slush and acidified. The organic solvents were flash evaporated leaving behind a gummy solid which was stirred overnight with a solution of 1.7 g sodium bicarbonate in 100 ml water.

The bicarbonate solution was filtered and acidified with concentrated hydrochloric acid to yield after filtration and recrystallization from ethanol, 470 mg (1.37 mmoles or 6.9%) of 35, mp 187.7-189.0° (effervescence).

An attempt at scaling up the reaction gave less material. It was later found that the ethanol recrystallization is wasteful and benzene recrystallization was substituted.

Mass Spectrum: 342 (1%), 298 (16%), 220 (23%), 193

(23%), 192 (13%), 191 (13%), 165 (10%), 105 (21%), 103 (100%), 77 (29%).

Analysis for $C_{23}H_{18}O_3$:

element	calculated	found
C	80.68%	80.20%
H	5.30%	5.52%

NMR ($CDCl_3$):

τ1.76-2.0	multiplet	2H	
2.20-2.97	multiplet	13H	
6.48	AB-quartet	2H	J_{AB}=8.0 Hz
-1.4	v. br. singlet	1H	

Infrared (KBr): 2940, 2510, 1730, 1630, 1590, 1570, 1460, 1250, 1240, 955, 750, 720, 710, 695, 690 cm^{-1}.

D) Using standard technique, diphenylcadmium was synthesized from 9.72 g (400 mmoles) of magnesium, 47.1 g (300 mmoles) of bromobenzene, and 31.2 g (281 mmoles) of anhydrous cadmium chloride.

The diphenylcadmium was leached from its reaction mixture with two 100 ml portions of benzene, filtered, and mixed with 8.98 g (34.0 mmoles) of 34 in 300 ml of benzene to yield, after standing for 36 hours, a gummy precipitate to which was added 90g (910 mmoles) of 37% hydrochloric acid in 500 ml of ice-water slush. The benzene layer yielded yellow crystals which were stirred overnight with a solution of 8.4 g (100 mmoles) of sodium bicarbonate in 600 ml of water. Acidification of the aqueous solution produced very little of the desired ketoacid as the residue left behind from the

bicarbonate wash contained most of the compound. The total yield was 2.45 g (7.17 mmoles or 21%) of the colorless, crystalline 35, mp ca. 190° (effervescence).

Analysis for $C_{23}H_{18}O_3$:

element	calculated	found
C	80.68%	80.48%
H	5.30%	5.43%

E) Phenylmagnesium bromide (39.5 mmoles) was prepared by standard technique in 75 ml of diethyl ether and added over 45 minutes to 10.4 g (39.4 mmoles) of 34 in 1200 ml of dry toluene which had been cooled to -68 to -75°. The reaction mixture was subjected to Maier's workup using 8.6 g (87.3 mmoles) of 37% hydrochloric acid in 500 ml of water and 8.4 g (100 mmoles) of sodium bicarbonate in 600 ml of water. As in D), some of the ketoacid did not dissolve in the bicarbonate at first and had to be dissolved in the bicarbonate solution after a crystallization from benzene. The total amount of material, 1.494 g (4.37 mmoles or 11.1%) was obtained in two crops, 735 mg and 759 mg, melting at, respectively, 197-198° and 188.5-189.5° (effervescence).

Pyrolysis of 35

A sample of 100 mg (0.292 mmoles) of 35 was heated neat at about 200° until gas evolution ceased. The brown melt was recrystallized twice from diethyl ether-light petroleum ether to yield 14 mg (0.047 mmoles or 16%) of slightly yellow needles, mp 125.0-125.7°, (lit.,[26] mp 126-126.5°). A separate

sample was pyrolyzed neat in an NMR tube to give the NMR spectrum described below. The compound was identified as 1,4,4-triphenylbut-3-en-1-one (48).

NMR ($CDCl_3$):

τ2.05-2.31	multiplet	2H	
2.42-3.0	multiplet	13H	
3.59	triplet	1H	J=7.0 Hz
6.21	doublet	2H	J=7.0 Hz

Infrared (KBr): 2900, 1670 (lit.[26], 1690), 1435, 1330, 1210, 995, 770, 765, 745, 700, 695, 685 cm^{-1}.

2,7,7-Triphenyl-3,4-diazabicyclo[4.1.0]hepta-2-en-5-one (36)

To 4.3 ml (4.3 g, 86 mmoles) of hydrazine hydrate in 400 ml of absolute ethanol was added 2.470 g (7.222 mmoles) of 35. After stirring for 12 hours a precipitate appeared and was filtered off after another 24 hours of stirring to yield 1.77 g (5.22 mmoles or 72.4%) of colorless crystals of 36 mp 244.0-245.0°. An analytical sample was obtained on recrystallization from ethanol, mp 244.7245.2°.

Mass Spectrum: 339 (5%), 338 (24%), 337 (16%), 235 (39%), 193 (22%), 192 (100%), 191 (28%), 166 (13%), 165 (47%), 115 (12%), 77 (13%).

Analysis for $C_{23}H_{18}N_2O$:

element	calculated	found	
C	81.63%	79.50%	79.63%
H	5.36%	5.71%	5.63%
N	8.28%	----	8.04%

Calculated for hemihydrate: C, 79.51%; H, 5.51%; N, 8.07%.

NMR ($CDCl_3$):

τ1.9	br. singlet	1H	
1.95-2.13	multiplet	2H	
2.40-3.16	multiplet	13H	
6.88	AB-quartet*	2H	J_{AB}=8.0 Hz

*The upfield half appears as a doublet of doublets due to further splitting by the N-H function. J_{BN}=1.5 Hz and J_{AN}=0.0 Hz as determined from an HA-100 spectrum.

Infrared (KBr): 3100, 3000, 2850, 1670, 1495, 1445, 1365, 1320, 1070, 775, 760, 705, 692 cm^{-1}.

2,5,7,7-Tetraphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (29)

Phenyllithium (9.94 mmoles) prepared from 197 mg (28.4 mmoles) of lithium and 2.23 g (14.2 mmoles) of bromobenzene in 60 ml of dry diethyl ether was added dropwise to 674 mg (1.99 mmoles) of 36 in about 100 ml of freshly distilled tetrahydrofuran (THF). The transient red color which appeared as each drop of phenyllithium made contact with the THF solution remained after about one-fifth of the addition.

The deep red reaction mixture was stirred an additional 30 minutes and then poured onto 500 ml of ice-water slush containing 800 mg (13 mmoles) of glacial acetic acid. The pale yellow compound was extracted with diethyl ether and chromatographed over basic alumina to yield 374 mg (0.939 mmoles or 47.2%) of bright yellow, beautiful needles of 29, mp 227.0-227.5° (dec.).

Mass Spectrum: 400 (1%), 399 (14%), 398 (40%), 370 (39%), 296 (25%), 295 (100%), 294 (23%), 193 (22%), 192 (18%), 166 (25%).

Analysis for $C_{29}H_{22}N_2$:

element	calculated	found
C	87.40%	87.44%
H	5.57%	5.58%
N	7.03%	6.93%

NMR ($CDCl_3$):

τ1.60-2.0	multiplet	4H
2.34-2.7	multiplet	6H
2.71	singlet	6H
3.03	singlet	6H
6.58	singlet	2H

Infrared (KBr): 2940, 1540, 1495, 1450, 1395, 765, 755, 705, 690 cm^{-1}.

Acid-catalyzed Rearrangement of 29

A sample of 100 mg of 29 was refluxed 3 hours in 50 ml of dioxane containing 0.5 ml of 37% hydrochloric acid to yield a bright yellow solution which, after neutralization, removal of solvent, and chromatography over basic alumina, yielded 46 mg (46%) of 3,6-diphenyl-4-benzhydrylpyridazine (33) as proved by NMR. The still colored 33 was recrystallized from absolute ethanol to give material melting 177.5-179°C (pure material, 185.7-186.0°).

Attempted Base-catalyzed Rearrangement of 29

A mixture of 93 mg of 29 and 19 mg of sodium hydroxide was refluxed for 75 hours in 25 ml of absolute ethanol to give a still green, but cloudy mixture which, after filtration and chromatography over basic alumina, yielded 73 mg (78% recovery) of 29, mp 231-231.5° (dec.). The NMR spectrum of the recovered material was identical to that for authentic 29.

Thermal Rearrangement of 29

A) A sample of 100 mg of 29 was refluxed a total of 24 hours in 25 ml of xylene. After flash evaporation of the xylene and chromatography over basic alumina, 45.1 mg (45.1%) of faintly colored unknown 49, mp 225.0-225.3° was obtained

B) A sample of 300 mg of 29 was refluxed for 23 hours in xylene containing a small amount of quinoline as a proton scavenger to yield 245 mg (81.7%) of 49 on crystallization from low-boiling petroleum ether.

Compound 49 was found to be unchanged on dissolving in pyridine. That the signal in the NMR spectrum of this compound in $CDCl_3$ at τ0.18 was due to hydrogen attached to nitrogen was proved by adding deuterium oxide to the NMR solution causing the signal to disappear.

Mass Spectrum: 400 (5.5%), 399 (32%), 398 (100%), 397 (14%), 321 (17%), 295 (3.5%).

Analysis for $C_{29}H_{22}N_2$:

element	calculated	found	
C	87.40%	87.34%	87.37%
H	5.57%	5.65%	5.61%
N	7.03%	7.02%	6.95%

NMR ($CDCl_3$):

τ0.18	br. singlet	1H
2.40-2.95	multiplet	15H
2.95-3.52	multiplet	6H

NMR (d_5-pyridine):

τ1.9-2.3	multiplet	4H
2.3-2.9	multiplet	12H
3.06	singlet	5H

Infrared (KBr): 3100, 2940, 1490, 1140, 970, 787, 773, 765, 750, 739, 729, 700, 693 cm^{-1}.

UV (ethanol): 298 (infl.), 255 (infl.), 237 (28400) nm.

Attempted Oxidation of 49

A) A sample of 106 mg (0.266 mmoles) of 49 was dissolved in about 4 ml of glacial acetic acid and 31.2 mg (0.106 mmoles) of potassium dichromate in 0.5 ml of water were added. The resulting orange solution was heated on the steam bath to give, after 2 hours, a dark green solution. Water was added to precipitate the organic material which was extracted into chloroform and chromatographed over basic alumina to yield mainly tar and 43.8 mg (41.3% recovery) of starting material, mp 225-226°. The NMR spectrum of the recovered material was identical to that for authentic 49.

B) A mixture of 75.0 mg (0.188 mmoles) of 49 and 44.7 mg (0.197 mmoles) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was refluxed for 1 hour in benzene to produce a very dark green, fairly insoluble compound which on chromatography

over basic alumina yielded 65 mg (0.16 mmoles or 8.7% recovery) of starting material, mp 225.5-226.0°. The mass spectrum of the recovered 49 showed no P-2 peak.

3-(4-chlorophenyl)-1,2-diphenylcyclopropene (62)

To 3.44 mmoles p-chlorophenylmagnesium bromide in 50 ml of dry diethyl ether was rapidly added 1.000 g (3.440 mmoles) of diphenylcyclopropenyl perchlorate. A resinous clump of brown material appeared immediately. After workup with saturated aqueous ammonium chloride and removal of solvent, the brown oil was chromatographed over basic alumina to yield a colorless, oily solid material which tended to discolor even in the absence of air and light. As determined at a later date, the desired material was probably obtained, but was contaminated with an unknown material which appeared to be produced by too rapid addition of the cyclopropenyl cation.

NMR ($CDCl_3$):

τ2.20-2.78	multiplet	12H
2.86	singlet	6H
6.79	singlet	1H

3-(4-methylphenyl)-1,2-diphenylcyclopropene (63)

A solid sample of 1.00 g (3.44 mmoles) of diphenylcyclopropenyl perchlorate was added slowly to a solution of 6.90 mmoles of p-tolylmagnesium bromide in 50 ml of diethyl ether under anhydrous conditions. As in the attempted synthesis of 62, rapid addition tends to produce resinous

material which discolors the final product. A mild reflux is produced on introduction of the cation to the Grignard reagent. After workup as in the case of 62 and chromatography over basic alumina, 451 mg (1.60 mmoles or 46.3%) of colorless, completely crystalline 63 was obtained, mp 103-105.5°. An analytical sample was obtained on recrystallization from hexane, mp 106.9-107.5°.

Mass Spectrum: 284 (4%), 283 (25%), 282 (100%), 281 (19%), 268 (12%), 267 (50%), 266 (11%), 265 (20%).

Analysis for $C_{22}H_{18}$:

element	calculated	found
C	93.58%	93.52%
H	6.42%	6.41%

NMR ($CDCl_3$):

τ2.04-3.25	multiplet	14H
6.83	singlet	1H
7.76	singlet	3H

Infrared (KBr): 2940, 1830, 1510, 1490, 1445, 1025, 915, 830, 763, 740, 688 cm^{-1}.

UV: 332.5 (23000), 315 (28000), 305 (s, 22000), 302 (infl.), 228 (32000) nm.

2,5-Bis(4-bromophenyl)-7-(4-methylphenyl)-1,6-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (66)

A mixture of 451 mg (1.60 mmoles) of 63 and 659 mg (1.68 mmoles) of 3,6-bis(4-bromophenyl)-1,2,4,5-tetrazine (65)[5] was refluxed for 55 hours in a 75:25 mixture of xylene-

chloroform to yield a wine-red reaction mixture which was filtered and chromatographed over basic alumina to yield 104 mg (0.265 mmoles) of recovered tetrazine 65 and, after long vacuum drying at elevated temperature, 777 mg (1.20 mmoles or 84.5% based on recovered tetrazine) of bright yellow crystals of 66, mp 231.5-232.0° with some resolidification and some decomposition.

Mass Spectrum: See Chapter II, Figure 6.

Analysis for $C_{36}H_{26}Br_2N_2$:

element	calculated	found
C	66.89%	67.12%
H	4.05%	4.18%
N	4.33%	4.31%

NMR ($CDCl_3$):

τ2.11-3.75	multiplet	22H
5.03	singlet	1H
7.83	singlet	3H

Infrared (KBr): 3000, 1590, 1490, 1390, 1320, 1070, 1010, 835, 725, 695 cm^{-1}.

Thermal Rearrangement of Diazanorcaradiene 66

A sample of 500 mg of 66 was refluxed in 100 ml of xylene for 24 hours to give a very pale yellow solution which was flash evaporated and chromatographed over basic alumina. Apparent unanticipated decomposition to pyrroles and benzonitriles made purification usually difficult and lowered the yield of crystalline diazepine 66. Only 130 mg (26%) of 66

mp 230.8-231.0° were obtained.

Mass Spectrum: See Chapter II, Figure 7.

Analysis for $C_{36}H_{26}Br_2N_2$:

element	calculated	found
C	66.89%	66.75%
H	4.05%	4.10%
N	4.33%	4.37%

NMR ($CDCl_3$):

τ2.36-3.33	multiplet	22H
4.20	singlet	1H
7.85	singlet	3H

Infrared (KBr): 2940, 1580, 1480, 1075, 1000, 1010, 840, 820, 805, 735, 720, 698 cm^{-1}.

X-ray Analysis of Diazepine 67

Crystals of the diazepine suitable for x-ray analysis were grown either from saturated chloroform-ligroin solutions or by solvent exchange using chloroform and ligroin. The diazepine crystallizes as beautiful, clear, almost colorless rhombs.

From precession photographs of a small crystal mounted along its diagonal, it was determined that the diazepine crystallizes in the monoclinic system with space group $C_{2/c}$ (C_{2H}^6) or C_c (C_S^4) (systematic absences hkl: h+k=2n; h0l: l=2n; 0k0: k=2n).[79] The rough cell constants were determined to be a=25.70 Å, b=10.48 Å, c=21.37 Å, and B=90°10'. A calculated density of 1.491 g/cm^3 assuming eight molecules

per unit cell agreed quite well with the experimentally found value (in carbon tetrachloride-cyclohexane) of 1.468 g/cm^3.

A crystal of approximate dimensions 0.207 x 0.275 x 0.25 mm was mounted on a Syntex Autodiffractometer for data collection. Molybdenum K_a radiation (0.71069 Å) was used. The accurate cell constants with their estimated standard deviations (e.s.d.) in parentheses next to them were determined by the diffractometer and are as follows: a=25.77 Å (0.01 Å), b=10.528 Å (0.009 Å), c=21.42 Å (0.02 Å), and β= 90.25° (0.02°). A total of 3872 reflections was measured by the 2θ-θ moving crystal-moving counter method up to 2θ = 45°.

After data processing, only 2643 reflections were considered observed, i.e. not less than 1.30 times their e.s.d. A Wilson plot[80] of the intensity data indicated that the diazepine probably crystallized with a centric space group ($C_{2/c}$).

A sharpened Patterson function[81] revealed the positions of the two bromine atoms thus solving the phase problem.

From a first Fourier series[82] on the data using the known positions of all the bromines, the positions of all thirty-eight non-hydrogen atoms were found and estimated by Booth's[83] method bringing the R-value to 34.051% in a second Fourier series. The same estimating procedure in the second Fourier brought the R-value down to 20.955%

Further refinement of the structure was accomplished using full-matrix least squares (FMLSQ) with all atoms

isotropic. After one cycle, the R-value dropped to 14.372%. After one more cycle of isotropic FMLSQ and one cycle of FMLSQ with only the bromine atoms anisotropic, the R-value dropped to 8.664% and, with all atoms anisotropic and three cycles of block diagonal least squares (BDLSQ), the R-value was 7.223%.

From a difference Fourier, the position of each hydrogen was also found and estimated again by Booth's method. Two cycles of BDLSQ excluding the hydrogens caused the R-value to drop to a respectable 5.982%. A final cycle of BDLSQ including the hydrogens only brought the R-value down to 5.921%, but refined the carbon-hydrogen bond lengths to acceptable limits (0.89 Å to 1.11 Å).

An ORTEP drawing of the molecule identified as 3,7-bis-(4-bromophenyl)-4-(4-methylphenyl)-5,6-diphenyl-4H-1,2-diazepine (67) is given in Chapter I along with a table of bond lengths and a table of bond angles and their e.s.d.'s.

7-(4-Methylphenyl)-1,2,5,6-tetraphenyl-3,4-diazabicyclo-[4.1.0]hepta-2,4-diene (68)

A mixture of 201 mg (0.712 mmoles) of impure 63 and 175 mg (0.748 mmoles) of 1 was stirred in 50 ml of chloroform for 14 days to yield a still purple solution which, on chromatography over basic alumina, gave 73.5 mg (0.150 mmoles or 21.1%) of bright yellow needles of 68, mp 212.8-213.0°.

Mass Spectrum: See Chapter II, Figure 9.

Analysis for $C_{36}H_{28}N_2$:

element	calculated	found
C	88.49%	88.38%
H	5.78%	5.85%
N	5.73%	5.62%

NMR ($CDCl_3$):

τ1.95-2.35	multiplet	4H
2.5-3.7	multiplet	20H
5.05	singlet	1H
7.85	singlet	3H

Infrared (KBr): 2940, 2850, 1490, 1440, 1330, 1070, 920, 810, 788, 775, 740, 725, 695 cm^{-1}.

2,5-Bis(4-iodophenyl)-1,6,7-triphenyl-3,4-diazabicyclo-[4.1.0]hepta-2,4-diene (71)

A mixture of 604 mg (1.24 mmoles, unchromatographed) of 17 and 367 mg (1.37 mmoles) of sym-triphenylcyclopropene[29] was refluxed for 12 days in 65 ml of a 10:3 chloroform-xylene mixture and then stirred at room temperature an additional 44 days in 50 ml of xylene. The resulting orange mixture was filtered and chromatographed over basic alumina to yield an undetermined amount of diazanorcaradiene 71 as bright yellow crystals, mp 223-224°.

Mass Spectrum: 728 (3%), 727 (12%), 726 (27%), 699 (18%), 698 (41%), 624 (14%), 623 (42%), 498 (31%), 497 (100%), 496 (23%), 493 (13%), 370 (13%), 368 (13%), 268 (13%), 267 (12%).

Analysis (crystallization from benzene-ligroin) for $C_{35}H_{24}I_2N_2$:

element	calculated	found	
C	57.87%	61.51%	61.61%
H	3.32%	3.97%	3.86%

Calculated assuming inclusion of 1 mole of benzene ($C_{41}H_{30}I_2N_2$): C, 61.21%; H, 3.75%.

Analysis (crystallization from chloroform-ligroin) for $C_{35}H_{24}I_2N_2$:

element	calculated	found
C	57.87%	51.77%
H	3.32%	3.08%
N	3.86%	3.33%

Calculated assuming inclusion of 1 mole of chloroform ($C_{35}H_{25}Cl_3I_2N_2$): C, 51.12%; H, 2.98%; N, 3.31%.

NMR ($CDCl_3$):

τ2.43	singlet	10H
2.5-3.3	multiplet	19H
5.02	singlet	1H

Infrared (KBr): 2950, 1580, 1500, 1480, 1500, 1480, 1450, 1390, 1320, 1010, 828, 757, 722, 695 cm^{-1}.

3,6-Dicyclopropyl-1,2,4,5-tetrazine (79)

A mixture 10.000 g (0.149 moles) of freshly distilled cyclopropyl cyanide, 45 ml of absolute ethanol, 2.96 g (9.24 mmoles) of flowers of sulfur, and 30.74 g (0.614 mmoles) of hydrazine hydrate was refluxed for 2.5 hours giving a green mixture. The mixture was poured into 800 ml of water to produce a cloudy suspension which was immediately oxidized with 10.4 g (0.150 moles) of sodium nitrite and 20 ml of glacial acetic acid.

The violet, smelly mixture resulting from the sodium nitrite oxidation was extracted to colorlessness with methylene chloride. After drying over anhydrous sodium

carbonate, the purple methylene chloride layer was concentrated by distillation through a column packed with glass beads. Codistillation of the tetrazine was a definite problem.

The concentrated solution was passed through a 3' x 1/4" FFAP on DMCS treated Chrom-P column at 120° to produce pure, beautiful, violet needles, mp 45.5-46.5° without decomposition. Yield: 5.7% by glpc using biphenyl as an internal standard.

Attempts at purifying 79 by passing over SE-30 on DMCS treated Chrom-P and by high vacuum line manipulation were only moderately successful. Recrystallization was out of the question as the compound is apparently soluble in all organic solvents. As with all aliphatic tetrazines, 79 is very volatile.

Low temperature NMR work was done on this compound. The temperatures were determined from dial settings after a calibration check.

Mass Spectrum: 160 (6%), 101 (6%), 81 (10%), 77 (18%), 57 (18%), 43 (56%), 41 (53%), 32 (100%).

Analysis for $C_8H_{10}N_4$:

element	calculated	found
C	59.24%	58.90%
H	6.21%	5.93%
N	34.55%	34.39%

NMR ($CDCl_3$):

τ7.23-7.71	multiplet	2H
8.60-8.86	multiplet	8H

NMR (CCl_4):

τ7.25-7.72	multiplet	2H
8.54-8.88	multiplet	8H

NMR (diphenyl ether):

τ7.35-7.95	multiplet	2H
8.58-9.25	multiplet	8H

Infrared (film): 2940, 1440, 1345, 1240, 1100, 1060, 1040, 915, 890, 820, 690 cm^{-1}.

UV and Visible (cyclohexane): 568 (550), 550 (706), 543 (758), 553 (s, 692), 333 (575), 323 (infl.), 310 (1950), 274 (s, 619), 226 (20100) nm.

UV and Visible (ethanol): 537 (502), 314 (1780), 270 (505), 228 (20100).

2,5-Diphenyl-1,3,4-thiadiazole (84)

A mixture of 103 g (1.00 moles) of benzonitrile, 206 g (4.20 moles) of hydrazine hydrate, 300 ml of absolute ethanol, and 20 g (0.62 moles) of flowers of sulfur was refluxed 1.5 hours to yield a yellow-orange precipitate (mostly dihydrodiphenyltetrazine). The yellow-orange precipitate was filtered off and oxidized with excess anhydrous iron trichloride in acetone to yield mostly 3,6-diphenyl-1,2,4,5-tetrazine (1) which was recrystallized from benzene-methanol.

The purple mother liquor from the oxidation was treated with cyclopropene until no tetrazine remained. The resulting yellow diphenyldiazanorcaradiene 6 and colorless thiadiazole 84 were separated by Soxhlet extraction with hexane. The

thiadiazole 84 is slightly soluble in hot hexane whereas the diazanorcaradiene 6 is completely insoluble. The thiadiazole was brought to final purity by chromatography over basic alumina. About 3 g (2.5%) of beautiful, colorless plates of 84, mp 141.3-142.5° (lit.,[48] mp 141-142°), were obtained.

Mass Spectrum: 240 (6%), 239 (16%), 238 (92%), 136 (10%), 135 (100%), 121 (26%), 103 (13%), 77 (48%).

Analysis for $C_{14}H_{10}N_2S$:

element	calculated	found
C	70.56%	70.82%
H	4.23%	4.27%

NMR ($CDCl_3$):

τ1.80-2.20	multiplet	4H
2.36-2.68	multiplet	6H

3,6-Dicyclopropylpyridazine (80)

A sample of 397 mg (2.44 mmoles, glpc purified) of 79 was refluxed for 50 minutes in freshly distilled norbornadiene to yield a colorless solution from which the excess norbornadiene was removed by distillation. The resulting heavy oil was chromatographed over silica gel to give 399 mg (2.43 mmoles, 99.6%) of a tan solid which was further purified by passing through a 2' x 3/8" 5% FFAP on DMCS-treated Chrom-P column held at 130°. The colorless crystals obtained from the glpc melted at 66.0-66.5°.

Mass Spectrum: 160 (11%), 159 (100%).

Analysis for $C_{10}H_{12}N_2$:

element	calculated	found
C	74.96%	74.84%
H	7.55%	7.72%

NMR ($CDCl_3$):

τ2.92	sh. singlet	2H
7.81-8.23	multiplet	2H
8.78-9.10	multiplet	8H

Infrared (KBr): 3100, 1600, 1550, 1450, 1440, 1060, 985, 880, 820, 785 cm^{-1}.

UV (cyclohexane): 342 (299), 276 (1330), 225 (14800) nm.

UV (ethanol): 317 (s,·248), 278 (1550), 226 (13400) nm.

3,6-Di-iso-propyl-1,2,4,5-tetrazine (88)

Sulfuric acid dried hydrogen chloride gas was bubbled into a mixture of 173.8 g (2.52 moles) of iso-butyronitrile and 116 ml of absolute ethanol at 0° until an increase in weight of 90 g (7.47 moles) was observed.

Crystallization of the imidate ester could not be induced so a yield of 324 g (2.14 moles, 85%) of iso-butyronitrile ethyl imidate ester hydrochloride was assumed and the imidate ester was converted into 1,2-dihydro-3,6-di-iso-propyl-1,2,4,5-tetrazine by addition of 69.8 g (2.18 moles) of anhydrous hydrazine in 150 ml of absolute ethanol at -60° over 1 hour under nitrogen, with stirring. Further stirring for 0.5 hours at -60° and 17 hours at room temperature completed the reaction.

Without isolation, the dihydrotetrazine was oxidized by

adding the reaction mixture containing the dihydrotetrazine to 4 liters of ice water containing 209.7 g (3.04 moles) of sodium nitrite, 152 g of glacial acetic acid, and 450 ml of methylene chloride. After separation and drying, the purple methylene chloride solution was concentrated by distillation through a packed column. Removal of as much remaining starting nitrile as possible was effected by vacuum pumping. As in the case of 79, codistillation of tetrazine was a problem. Crude yield: 47.7 g (90% pure via glpc, 0.287 moles, 22.8%) of a deep purple oil. Final purification for spectral purposes was effected by passing through a 2' x 1/4" FFAP on DMCS-treated firebrick column at 60°C. Tetrazine 88 was never obtained in a crystalline state.

Mass Spectrum: 168 (1.5%), 167 (2.5%), 166 (21%), 70 (91%), 69 (34%), 68 (56%), 54 (46%), 43 (100%), 42 (93%), 41 (13%).

NMR (CCl_4):

τ6.40	septuplet	2H	J=7.0 Hz
8.48	doublet	12H	J=7.0 Hz

Infrared (film): 2940, 1450, 1390, 1360, 1345, 1320, 1270, 1230, 1150, 1070, 1060, 890, 875 cm^{-1}.

UV and Visible (cyclohexane): 576 (s, 392), 552 (537), 280 (infl.), 271 (3020) nm.

UV and Visible (ethanol): 544 (460), 273 (2920) nm.

3,6-di-iso-propyl pyridazine (89)

A mixture of 29.7 g (assumed 90% pure, 0.161 moles) of

88 and 47 g (0.51 moles) of norbornadiene was refluxed for 7.5 hours at the end of which time all color due to the tetrazine had disappeared. After removal of excess norbornadiene and dicyclopentadiene, the resulting crystalline slush was chromatographed over basic alumina and then recrystallized from hexane at dry ice temperatures to yield two crops of crystals, mp 75.0-76.5°, and weighing a total of 10.6 g (0.0645 moles or 39.8%). The second crop was slightly tan. Material recrystallized several times from diethyl ether melted at 77.5-79.0°. Vacuum sublimation and glpc separation on a 5% FFAP column at 120°C only served to lower the melting point.

Mass Spectrum: 165 (3%), 164 (17%), 163 (25%), 151 (12%), 150 (100%), 146 (84%), 144 (11%), 121 (10%), 41 (11%).

Analysis for $C_{10}H_{16}N_2$:

element	calculated	found
C	73.12%	73.08%
H	9.82%	9.95%
N	17.06%	16.83%

NMR (CCl_4):

τ2.65	sharp singlet	2H	
6.75	septuplet	2H	J=7.0 Hz
8.65	doublet	12H	J=7.0 Hz

Infrared (KBr): 3100, 3000, 1580, 1450, 1420, 1370, 1280, 1160, 1140, 1060, 1055, 1040, 1020, 865, 805 cm^{-1}.

UV (cyclohexane): 344 (290), 262 (1720), 257 (1670) nm.

UV (ethanol): 320 (227), 257 (1650) nm.

Pyrolysis of 68

With the glpc injector at 260° and a 5' 6% XF-1150 column at 90°C (the column temperature at which p-tolunitrile and benzonitrile were well separated), 2 µl of 68 in benzene (saturated) were injected into the Hy-Fi instrument. Both p-tolunitrile and benzonitrile peaks were observed. Tailing was a problem as was expected. The peaks were identified solely on the basis of retention times. No attempt was made to determine the relative amount of each nitrile.

Reaction of diazanorcaradiene 6 with DDQ

A solution of 899 mg (3.96 mmoles, benzene dust-free filtered and freshly recrystallized from chloroform) of DDQ in 80 ml of dry benzene (orange solution) and a solution of 975 mg (3.96 mmoles, chloroform dust-free filtered and freshly recrystallized from chloroform-ligroin) of 6 in 90 ml of dry benzene (bright yellow solution) was mixed to form a very deep red solution which was refluxed 30 minutes and allowed to sit overnight at room temperature. After sitting overnight, 797 mg of almost jet black crystals of unknown (94) crystallized.

After filtering off the dark crystals, the reaction was returned to reflux for 2 more hours and allowed to cool. Upon cooling, another 474 mg of brown, but crystalline material precipitated.

Mass Spectrum: 246, 245, 230, 228, with peaks at as high a mass as 486.

Analysis for $C_{25}H_{14}Cl_2N_2O_2$:

element	calculated	found
C	63.44%	64.96%
H	2.98%	3.41%
N	11.84%	11.22%
Cl	14.98%	13.22%

NMR (trifluoroacetic acid):

τ1.6-2.8	br. multiplet
2.70	singlet

Infrared (KBr): 2960, 2190, 1620, 1590, 1550, 1540, 1440, 1400, 1380, 1270, 1200, 890, 780, 765, 695 cm^{-1}.

Attempted Reaction of 3,6-diphenyl-4-methylpyridazine[3] (95) and DDQ

A solution of 50 mg (0.203 mmoles) of 95 and 45.1 mg (0.203 mmoles) of DDQ in 50 ml of benzene was refluxed for 75 minutes with no perceptible change. No change or precipitate was found on allowing the mixture to stand overnight.

Attempted Reaction of 6 and Trityl Fluoroborate

A solution of 100 mg (0.406 mmoles) of 6 in 100 ml of acetonitrile was mixed with 134 mg (0.406 mmoles) of fresh trityl fluoroborate. There was no noticeable change. Heating produced nothing but what is assumed to be tar.

Attempted Reaction of Diphenylcyclopropenone[77] with 9

A mixture of 206 mg (1.00 mmole) of diphenylcyclo-

propenone[77] and 198 mg (1.00 mmole) of 9 in 25 ml of methylene chloride was allowed to stir at room temperature for 48 days. The resulting yellow mixture yielded white solid on addition of low boiling petroleum ether. After chromatography over deactivated alumina, the white solid appeared to be an impure sample of diphenylcyclopropenone.

Attempted Bromination of 3,4,5,6,7-Pentaphenyl-4H-1,2-diazepine (3)[2]

A solid sample of 237 mg (0.500 mmoles) of 3 was suspended in 250 ml of carbon tetrachloride and a small amount of bromine was added. After stirring for 2 days, the suspension dissolved and then deposited yellow crystals of 97 which, on workup, gave an NMR spectrum very similar to that of the starting material 3. The material 97 was tentatively identified as the N-bromo bromide salt of 3. No attempt at obtaining an elemental analysis or mass spectrum was made due to the instability of the material.

NMR ($CDCl_3$):

τ2.15-2.4	multiplet	2H
2.46-3.25	multiplet	23H
3.95	br. singlet	1H

Diphenylcyclopropenone Ethylene Ketal (106)[78]

A solution of 3.1 g (15 mmoles) of diphenylcyclopropenone[77] in 3.8 ml of dry methylene chloride was added to a solution of 3.0 g (16 mmoles) of triethyloxonium fluorobroate in 5 ml of dry methylene chloride. The combined solutions,

which sometimes crystallized, were added to 750 mg (33 mmoles) of sodium dissolved in 19 ml of dry ethylene glycol at 10-20°. The workup was that described in the literature[78] except that the major portion of the ketal was found in the cyclohexane mother liquor rather than the first crop of crystals. The ketal had properties which agreed with those in the literature.[78]

Attempted Cycloaddition of 9 with 106

Under anhydrous conditions 250 mg (1.00 mmoles) of 106 and 188 mg (0.950 mmoles) of 9 were stirred in 25 ml of methylene chloride for 2 days and then, due to the sluggishness of the reaction, refluxed in chloroform for 3 days to yield an orange oil which turned dark green in the vacuum desiccator. Chromatography of the green oil over deactivated alumina gave unidentified blue, yellow, and dark green bands.

Attempted Preparation of Dimethyl 4,6-Diphenyl-3,7-dicarboxy-1,2-diazepin-5-one

A mixture of 141 mg (0.919 mmoles) of potassium dihydrogen phosphate as a saturated aqueous solution, 250 mg (0.691 mmoles) of 22, 79.5 mg (0.689 mmoles) of selenium dioxide, and 5 ml of dioxane was combined at which time the color of the diazanorcaradiene 22 was discharged. The still faintly yellow suspension was maintained at 90-93°C for 21 hours, filtered, washed with water, extracted with methylene chloride, and concentrated to yield a yellow oil which gave no identifiable peaks in the NMR. Chromatography over deactivated alumina also gave no identifiable product.

Reaction of 26 with Trityl Perchlorate

A solution of 343 mg (1.00 mmole) of trityl perchlorate in 15 ml of dry methylene chloride was mixed with 322 mg (1.00 mmole) of 26 in 10 ml of dry methylene chloride under anhydrous conditions and stirred for 14 hours at which time a precipitate had been formed. The precipitate was filtered and washed with a small amount of methylene chloride to yield 129 mg (0.305 mmoles or 30.5%) of bright yellow microneedles, mp 213.7-213.9° (dec.). The compound was identified as 3,5,7-triphenyl-4H-1,2-diazepine hydroperchlorate (98).

Analysis for $C_{23}H_{19}ClN_2O_4$:

element	calculated	found
C	65.32%	65.18%
H	4.52%	4.62%

NMR (TFA):

τ1.80-2.75	multiplet	17H
5.70	br. singlet	2H

Infrared (KBr): 3100, 1600, 1490, 1120, 1100, 1090, 770, 760, 695 cm^{-1}.

Reaction of 26 with Trityl Fluoroborate

Under anhydrous conditions, a saturated solution of 693 mg (2.10 mmoles) of trityl fluoroborate in dry methylene chloride was stirred with 645 mg (2.00 mmoles) of 26 in 20 ml of dry methylene chloride for 18 hours. Filtration yielded 293 mg (0.715 mmoles or 35.7%) of yellow crystals melting at 196-199° with decomposition. Chromatography of the dark

mother liquor yielded no triphenylmethane. The NMR sample of the compound in trifluoroacetic acid did not decompose or change even on standing for 22 days. The compound was identified as 3,5,7-triphenyl-4H-diazepine hydrofluoroborate (99).

Low temperature NMR work was done on this compound.

Mass Spectrum: 324 (4%), 323 (32%), 322 (95%), 220 (36%), 219 (100%), 218 (19%), 115 (15%), 103 (15%), 77 (12%), 49 (18%), 45 (20%).

NMR (trifluoroacetic acid):

τ1.80-2.75	multiplet	17H
5.70	br. singlet	2H

Infrared (KBr): 3100, 1600, 1490, 1125, 1100-1040, 1000, 970, 775, 695, 685 cm^{-1}.

Treatment of 99 with Sodium Borohydride

A small undetermined amount of the salt 99 was added to a solution of excess sodium borohydride in acetonitrile producing immediate gas evolution and decolorization. Solvent evaporation, washing with water, and extraction with chloroform yielded a pale green solid which melted at 193.0-193.8° (dec.) after recrystallization from ethanol.

The mixed melting point with an authentic sample of 3,5,7-triphenyl-4H-1,2-diazepine (26)[17] was 193.8-194.0° (dec.) The infrared spectrum of this material was identical to that for authentic 26.

3,5,7-Triphenyl-4H-1,2-diazepine Hydroperchlorate (98)

To an ice-cold solution of 0.18 ml (2.0 mmoles) of 70% perchloric acid in 20 ml of acetic anhydride was added, with stirring, a suspension of 644 mg (2.00 mmoles) of 26 in acetic anhydride. The orange solution, which was produced, was stirred for 1 hour and then poured into 300 ml of anhydrous diethyl ether. The crystalline solid was filtered and washed to a light yellow-orange with methylene chloride-diethyl ether. After drying the crystals gave mp 212.0-213.0° (dec.). The NMR spectrum of this compound was identical to that for the compound obtained on mixing trityl perchlorate and 3,5,7-triphenyl-4H-1,2-diazepine (26). No attempt was made at obtaining a yield for this reaction.

Attempted Preparation of Bis(dimethyl 1,6-diphenyl-3,4-diaza-bicyclo[4.1.0]hepta-2,4-dien-7-yl-2,5-dicarboxylate) Ether

To a stirred solution of 438 mg (1.10 mmoles) of bis(1,2-diphenylcyclopropen-3-yl) ether (109)[75] in 50 ml of methylene chloride was added 479 mg (2.20 mmoles) of solid 9 producing immediate nitrogen evolution for about the first 50% of the reaction at which time the reaction appeared to terminate. The reaction mixture which was still red was flash evaporated to yield 184 mg unreacted tetrazine. Dark yellow crystals of what at first was thought to be diazanor-caradiene were brought out of the benzene solution with light petroleum ether. Since the NMR showed a peak for what was assumed to be unreacted starting ether, the reaction was

continued with another 184 mg of tetrazine 9 in 50 ml of methylene chloride. Even after 4 more days of stirring there was no further change in the reaction mixture.

Attempted Preparation of 1,2-Diphenylcyclopropen-3-yl 1,6-Diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-dien-7-yl-2,5-dicarbomethoxy Ether (105)

A solution of 198 mg (1.00 mmole) of 9 in 20 ml of methylene chloride was added with magnetic stirring to 438 mg (1.10 mmoles) of 103[75] in 50 ml of 5:1 methylene chloride-diethyl ether resulting in slow but definite gas evolution and decolorization. After stirring overnight, the bright yellow solution was filtered, flash evaporated, dissolved in carbon tetrachloride and filtered again to remove 27 mg (0.068 mmoles) of what is assumed to be excess 103, mp 163-165°. The yellow carbon tetrachloride solution yielded a total of 373 mg (0.657 mmoles or 65.7%) of bright yellow crystals, mp 167.8-170.5°. Two recrystallizations from chloroform-light petroleum ether raised the melting point to 173.7-174.1°. The compound is tentatively identified as 4,5-dipheny-3,6-dicarbomethoxy-1-(1,2-diphenylcyclopropen-3-yl)-1,4-dihydropyridazine-4-aldehyde (104).

Mass Spectrum: 570 (1.5%), 569 (3.5%), 568 (10%), 540 (11%), 539 (25%), 482 (13%), 481 (34%), 465 (0%), 362 (0%), 350 (14%), 349 (55%), 206 (0%), 192 (21%), 191 (100%), 86 (30%), 84 (30%), 43 (18%), 42 (12%).

Analysis for $C_{36}H_{28}N_2O_5$:

element	calculated	found
C	76.04%	75.84%
H	4.96%	5.01%
N	4.93%	4.89%

NMR ($CDCl_3$):

τ1.08	sh. singlet	1H
1.93-3.23	multiplet	20H
5.32	sh. singlet	1H
6.42	sh. singlet	3H
6.52	sh. singlet	3H

Infrared (KBr): 2950, 2840, 2730, 1730, 1700, 1540, 1440, 1435, 1340, 1230, 1200, 1140, 780, 770, 760, 705, 692 cm^{-1}.

UV and Visible (chloroform): 590 (approx. 180), 377 (4880), 312 (infl.), 303 (26000), 298 (24600) nm.

Attempted Preparation of 3,5,7-Triphenyl-1,2-diazacycloheptatrienylium Cation

A solution of 645 mg (2.00 mmoles, dust-free, freshly recrystallized from ethanol) of 26 in about 75 ml of dry, dust-free benzene (pale green solution) was placed in a nitrogen-filled, oven-dried flask fitted with an addition funnel charged with 454 mg (2.00 mmoles, benzene dust-free filtered, freshly recrystallized from chloroform) of DDQ in about 35 ml of dust-free benzene (orange solution). As the DDQ solution was added to the diazepine solution, a deep red solution resulted. After about an hour of stirring, the

deep red solution slowly deposited needles of colorless material which yellowed slightly on isolation. A total of 972 mg (1.77 mmoles or 88.5%) of material (102) was isolated. The first crop melted at 178.0-178.5° with extensive decomposition.

Mass Spectrum: 548 (trace), 546 (trace), 532 (3%), 430 (5%), 323 (24%), 322 (85%), 321 (20%), 308 (23%), 307 (79%), 306 (31%), 294 (13%), 232 (16%), 230 (79%), 229 (15%), 228 (97%), 220 (46%), 219 (100%), 218 (30%), 217 (17%), 215 (13%), 204 (13%), 202 (47%), 200 (67%), 191 (19%), 189 (13%), 137 (18%), 117 (13%), 116 (15%), 115 (31%), 110 (24%), 109 (13%), 103 (23%), 102 (15%), 101 (17%), 91 (16%), 89 (12%), 87 (34%), 77 (42%), 76 (16%), 51 (19%).

Analysis for $C_{31}H_{18}Cl_2N_4O_2$:

element	calculated	found	
C	67.77%	67.92%	67.91%
H	3.30%	3.39%	3.36%
N	10.20%	10.16%	10.17%
Cl	12.91%	12.79%	12.86%

NMR (TFA):

τ1.6-2.7 multiplet

Infrared (KBr): 2960, 2200, 1600, 1470, 1440, 1410, 1350, 1010, 1005, 930, 775, 760, 690 cm^{-1}.

UV (acetonitrile): 295 (s, 18000), 528 (31900), 221 (38100), 201 (53200) nm.

Reduction of Complex 94

A slurry of 160 mg (4.2 mmoles) of sodium borohydride in a small amount of acetonitrile was added to a deep red partial solution of 200 mg (0.422 mmoles) of 94 in 35 ml of acetonitrile producing immediate gas evolution and gradual color change to orange-yellow. The voluminous precipitate, which also resulted, was filtered and washed with chloroform. The chloroform-acetonitrile solution was extracted with water, dried, and concentrated. Addition of low boiling petroleum ether to the concentrated solution produced colorless crystals covered with yellow resin. Filtration and washing with a small amount of diethyl ether yielded 27.8 mg (0.112 mmoles or 26.5%) of almost colorless, very fine needles, mp 165.3-165.5. A recrystallization from chloroform-ligroin removed most of the color and raised the melting point to 166.0-166.5°. The NMR and infrared spectra of this compound were exactly identical to those for a sample of 2,5-diphenyl-3,4-diaza-bicyclo[4.1.0]hepta-2,4-diene (6) which had been subjected to sodium borohydride reduction.

Reduction 6

A sample of 500 mg (2.03 mmoles) of 6 was dissolved in 60 ml of acetonitrile by warming to produce a bright yellow solution. To this bright yellow solution was added with magnetic stirring 380 mg (10 mmoles) of sodium borohydride and 0.50 ml of water. No reaction occurred.

Addition of another 400 mg (106 mmoles) of sodium

borohydride and 1 ml of water produced immediate gas evolution and gradual decolorization. After 1.5 hours of stirring the reaction mixture was colorless and contained a voluminous, cottony precipitate. The acetonitrile was removed, the precipitate filtered, washed with water, and dried to a constant weight of 492 mg (1.98 mmoles or 97.6%) of cottony, almost colorless microneedles, mp 161.5-163°.

A recrystallization from chloroform-diethyl ether gave as a first crop 397 mg (1.60 mmoles) of snow-white microneedles, mp 166.7-168.0°. On standing, solutions of the reduction product 96 turn a greenish-yellow presumably due to air oxidation back to the diazanorcaradiene 6. Compound 96 is tentatively identified as 2,5-diphenyl-3,4-diazabicyclo-[4.1.0]hept-2-ene. No attempt has been made at assigning the stereochemistry of this compound.

Mass Spectrum: 250 (2.7%), 249 (22%), 248 (100%), 171 (26%), 157 (15%), 144 (20%), 143 (13%), 117 (19%), 115 (19%), 104 (11%), 91 (16%), 77 (14%).

Analysis for $C_{17}H_{16}N_2$:

element	calculated	found
C	82.22%	82.29%
H	6.50%	6.60%
N	11.28%	11.29%

NMR ($CDCl_3$):

τ2.1-2.43	multiplet	2H
2.43-2.92	multiplet	8H
4.59	v. br. singlet	1H
5.92	br. singlet	1H
7.75-8.15	multiplet	3H
8.8-9.1	multiplet	1H

Infrared (KBr): 3170, 2920, 2760, 1590, 1480, 1390, 1140, 1020, 1005, 852, 762, 752, 700, 688 cm^{-1}.

Attempted Oxidation of 104

To a yellow solution of 50 mg (0.088 mmoles) of 104 in about 3 ml of glacial acetic acid was added 3 drops of water and 10.7 mg (0.352 mmoles) of potassium dichromate. The orange solution thus produced was heated on the steam bath producing an immediate dark green color. After heating 2 hours, addition of water, extraction with chloroform, neutralization with sodium bicarbonate, and addition of ligroin only resinous material was produced. Dissolving the resinous yellow oil in diethyl ether and cooling only precipitated resin again.

2,5-Diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (6)[2]

Diazanorcaradiene 6 was prepared by the method of Battiste and Barton.[2] The NMR spectral data were recorded as given below.

NMR ($CDCl_3$):

τ1.6-2.0	multiplet	4H
2.25-2.65	multiplet	6H
7.05-7.45	multiplet	2H
7.65-8.05	multiplet	1H
9.5-9.85	multiplet	1H

NMR (TFA/$CDCl_3$):

τ1.75-2.0	multiplet	4H
2.0-2.6	multiplet	6H
6.4-7.15	multiplet	3H
8.95-9.25	multiplet	1H

3,6-Diphenylpyridazine (93)[1]

The known 3,6-diphenylpyridazine (93) was synthesized in only 60% yield by stirring 4.68 g (20.0 mmoles) of 1 in about 15 ml of freshly distilled norbornadiene for 2.5 hours at room temperature. Crystallization of the desired pyridazine was induced by the addition of 150 ml of hexane to the reaction mixture.

NMR ($CDCl_3$):

τ1.72-2.02	multiplet	4H
2.10	singlet	2H
2.32-2.67	multiplet	6H

UV (ethanol): 279 (29300).

"Who are you? What have you sacrificed?"

Jesus Christ Superstar, 1970

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BIOGRAPHICAL SKETCH

Robert Merrifield White was born July 24, 1945, at Terre Haute, Indiana. In June, 1963, he was graduated from Huntsville High School, Huntsville, Alabama. In June, 1967, he received the degree of Bachelor of Arts with a major in Chemistry from Vanderbilt University. Upon receiving the Bachelor of Arts degree, he was also commissioned as a second lieutenant in the United States Army Signal Corps. In 1967 he enrolled in the Graduate School of the University of Florida. During his pursuit of the degree of Doctor of Philosophy he has held both teaching and research assistantships. From September, 1967, until the present time he has pursued his work toward the degree of Doctor of Philosophy.

Robert Merrifield White is married to the former Ann Marie Bischof, and is the father of one child. Mr. White is a member of Eta Sigma Phi, National Honorary Classical Fraternity; Scabbard and Blade, Alpha Chi Sigma, chemists' fraternity, and The American Chemical Society.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

Merle A. Battiste

Merle A. Battiste, Chairman
Professor of Chemistry

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William Weltner, Jr.

William Weltner, Jr.
Professor of Chemistry

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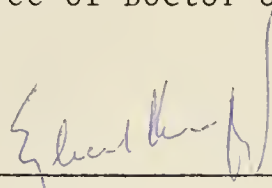

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This dissertation was submitted to the Department of Chemistry in the College of Arts and Sciences and to the Graduate Council, and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

March, 1972

Dean, Graduate School

"And I think I shall sleep well tonight
Let the world turn without me tonight."

Jesus Christ Superstar, 1970